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OF THE

NATIONAL MALARIA SOCIETY

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OF THE
National Malaria Society

VOLUME II 1943 Number 1

INCLUDING PROCEEDINGS OF THE XXV ANNUAL MEETING

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NOTICES

The Society plans to expand the Journal to a quarterly of approximately 50 pages per issue as soon as financial support and sufficient contributed material justify such action. At that time application will be made to the postal authorities for second class mail rates.

Material for Submission:

Contributed papers on any phase of malaria or related subjects should be submitted to the editor. If suitable papers contain tables, require illustrations, or will require more than six pages in the Journal for publication, acceptance will be contingent upon the willingness of the contributor to assume the extra cost entailed by special typesetting; manufacture of cuts or over-run, which amounts are to be paid directly to the printer. Orders for reprints should be placed with the printers, and are to be attached to the galley proof when it is returned to the editor.

Pertinent advertisements will be accepted from reputable firms. Correspondence in relation thereto should be addressed to the secretary-treasurer.

Subscriptions

The Journal will be sent at time of publication to all members of the National Malaria Society whose dues for the current year are paid. It will be supplied members then in arrears when they terminate the delinquency.

Subscriptions will be received from non-members and institutions at the rate of three dollars per annum from domestic subscribers, and three dollars and fifty cents from foreign subscribers. Subscriptions should be placed with the secretary-treasurer.

Revenue accruing to the Society from subscriptions will be wholly utilized for the support and enlargement of the Journal.

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THE WAR AND OUR OPPORTUNITY FOR SERVICE

Presidential Address

John H. O'Neill

Our organization came into being as the National Malaria Committee, twenty-six years ago, in the midst of a World War.

Shortly after its organization our country entered the war, and our membership in various capacities contributed their services to the ultimate victory.

During the past quarter of a century there has been a very considerable advance in our knowledge of malaria, its means of spread and methods of control.

Many individual members of the Society, and some of our committees, have made important contributions to this advance, and the work of other committees has helped us all to keep well informed and to apply newer knowledge in a practicable and effective manner.

We are now engaged in another World War incomparably greater in size, extent and potentialities. It is, as has been said so often, a total war. Too frequently, perhaps, that statement is made lightly, without adequate realization that it is stark and absolute truth.

The dominant purpose of every individual and of every organization for the duration of this emergency should be to render all possible aid to winning the war.

Many of our members are making direct and personal contributions to the war.

It is but timely and fitting that we, as a group, should review our activities and committee organization with a view to determining whether we can make more effective contributions to the war effort and to the planning for post-war needs.

I have reviewed the assignments to our committees and respectfully submit for your consideration some comments and suggestions.

The function of our Committee on Medical Research is "to review and promote research in the parasitological, the chemical, and the therapeutic phases of malaria, and to stimulate efforts at more satisfactory prophylaxis and treatment."

The annual reports of the committee have kept us well informed of developments along these lines, all over the world.

It is just about three hundred years ago that cinchona bark was introduced into Europe, and even today quinine is the most

generally used anti-malaria drug. Since our enemies are in posession of the lands from which came our supplies of quinine, there is a shortage of this valuable drug, and the shortage will become more and more acute. It is imperative that there be a prompt development of plentiful supplies of quinine and of acceptable substitutes for quinine. Considerable work is being done toward this objective, and it appears probable that we may soon have some potent (sulfa) compounds to supplement the atabrine and plasmochin which have been found so useful.

It is desirable also to promote cinchona culture in accessible areas, even though it would take some years to bring the trees to productiveness.

A forester friend has told me that he had some young trees growing well in central Louisiana up to 1939, when they were killed by a freeze when the temperature went below 29° F. He is of the opinion that cinchona trees will grow in the Brazos Valley in Texas and in some sections of Mexico. I have been informed that our Forestry Service is to send an expedition to South America which will give consideration to sources of quinine as well as to other matters.

The War Production Board in its fifth provisional report (August 21, 1942), on relative scarcity of certain materials, listed quinine in "Group I—Materials of which the supplies are inadequate for war and most essential uses."

Since June 19th the sale and use of quinine and totaquine has been limited to use as anti-malaria agents and, in the case of quinidine, for the treatment of cardiac disorders.

The present situation regarding rubber suggests some questions.

Are we likely to suffer from a shortage of anti-malaria drugs?

Are our government agencies doing *all* that should be done to promote and ensure the development of adequate supplies of anti-malaria drugs for the war and for the post-war period, at a price which the sick can afford to pay?

These are pertinent questions and are within the scope of the committee's function. Perhaps the committee may be able to evaluate the possibilities in this matter and—if it appears desirable —the Society might take steps to promote action so that it will not be necessary to say of the development of anti-malaria drugs:— "too little and too late".

On the other hand, if the situation is satisfactory, a statement from the Committee to that effect will be welcome.

It is probable that the rubber situation might be quite different

today if a committee of a non-partisan organization, e. g., a national society of technical experts, had surveyed the situation and issued a report early in 1941.

The assignment to the Committee on Entomology is to review and promote the collection of entomological data bearing on malaria problems.

That covers a lot of territory. The committee has given us some fine reports, and has kept us well informed regarding the literature on this particular item. Comments from entomologists presently engaged in control work suggest that reports on special topics would be helpful at this time, for example:—(a) one referred to Bellamy's excellent article[1] dealing with various aquatic growths as indication of potential breeding of *A. quadrimaculatus* with the statement that there appeared to be variations in such correlation in other sections of the South, and he suggested that the committee might make a survey by questionnaire to entomologists in other states to promote the collection of further data on this subject; (b) another pointed out that not only will our returning troops bring back malaria infection, but that the present greatly increased air traffic between the United States and the malarious areas of the world will increase the possibility of introducing alien Anophelines. Information regarding species that might possibly be introduced into the United States and breed here is scattered through a considerable amount of literature. It has been suggested that a report summarizing, for the more important such species at least, description and breeding habits would be very helpful to entomologists engaged in control work in our southern states.

The report of the group of malariologists called together by the Surgeon General of the United States Public Health Service in 1940, for the purpose of considering some of the fundamental aspects of malaria research and of exploring opportunities for stimulating its extension and coordination, suggests a number of potentially valuable studies.[2]

The work of the Committee on Sanitary Engineering is very similar to the work of the Committee on Mosquito Control of the Conference of State Sanitary Engineers.

The report of Malaria Control for Engineers, prepared by the joint committee of our Society and the Sanitary Engineering Division of the American Society of Civil Engineers has been very valuable in presenting the subject to engineers.[3]

It is suggested that consideration be given to developing closer liaison with the Conference of State Sanitary Engineers through

organization of a joint committee with a view to affording opportunity for greater cooperation, and avoiding duplication of effort.

We have troops located in most of the tropical and semi-tropical regions of the world. Some units are in highly malarious areas. In some of these areas British experience has shown that troops unprotected for one night will develop a 20% incidence; and unprotected for two nights, a 30% incidence.

Anti-malaria measures of all sorts are, of course, being used. One of the items of especial concern at the present time is the problem of "building out" malaria, through proper procedures and precautions, in our foreign bases and airfields. There is needed a manual with simple, practicable construction plans and specifications which could be issued to engineers and construction crews. I have been given information, at present unofficial, that officers studying this problem would be glad to have a committee of the Society working informally with them on this and other subjects. It is recommended that a special sub-committee be appointed to develop a program for cooperation with the Army.

Practically all present malaria prevention activities conducted by governmental agencies in the United States are included, and rightly so, in the campaign for malaria control in war areas. Our program for today consists of a symposium on this topic.

Let us consider briefly plans for the post-war program—with the fervent, but probably over-optimistic, hope that we may discuss, at our next meeting, a progress report on this topic that will really be a post-war report.

The map in the third edition of Craig and Faust's "Clinical Parasitology" showing the distribution of malaria throughout the world looks very much like a map of the world showing the areas of military and political activity of World War II. Some of the areas of present military activity and of probable future activity are very highly malarious. It is reported that one of the worst malaria epidemics in the history of Delhi province (India) occurred this year, and that at its height nearly 7,000 persons were hospitalized weekly.

Many of our returning troops will bring back malaria infections and other tropical diseases. There are many places in the United States with Anopheles mosquitoes but without malaria. Soldiers returning from malarious areas with infection may give rise to outbreaks of malaria in such areas.

The success of the malaria-mosquito control work around army camps and cantonment towns in World War I was convincing proof

that malaria control in southern states by control of Anopheles was not only theoretically possible, but was also economically practicable.

This large scale demonstration, the availability of a large group trained by this experience, in mosquito control methods and financial assistance from the Rockefeller Foundation and the United States Public Health Service made possible a rapid expansion after the war, of the program which had been started a few years earlier by the United States Public Health Service, in the form of demonstration studies in urban and rural sections of the South.

State Boards of Health in the South should plan now to convert the present campaign of malaria control in war areas into a major and more extensive post-war activity.

It seems quite probable that there will be an acceleration of industrial development in the South after the war. It does not seem likely that Boards of Health will get the sort of financial assistance that they received after the last war, but rather that malaria control costs must come from taxes. The support of Industry will be essential for such a program.

The present campaign of malaria control in war areas includes mosquito control around war industries. The results should be influential in selling malaria control to Industry, if properly presented. Our Committee on Industrial Relations could be of help in such a sales campaign. It is suggested that consideration be given to a revision of the functions assigned to the committee, to meet more fully present day conditions and future needs.

Both the Committee on Statistics and the Committee on Industrial Relations are concerned with data relating to the economics of malaria. It is rather difficult for the average industrialist to interpret community vital statistics in terms of a profit and loss account related to his own business .

A very different situation exists in the field of industrial safety. Under the leadership of the National Safety Council, and with the aid of insurance companies, statistics have been compiled for different industries and for different occupations in terms of frequency rates (i.e., number of lost time injuries per one million man-hours) and severity rates (i.e., time loss in days, per 1,000 man-hours).

The value of wages for lost time, the value of lost productivity, cost of medical care and of compensation payments, etc., represent *direct* cost of accidents to Industry. In addition, authorative studies indicate that hidden costs are equal to four times the direct costs.

Van Hovenberg[4] gave us some very valuable information of this sort over twenty years ago, and we have had some from other

sources, but we need more of it based on current experience; and it would be desirable to have it expressed in a form directly comparable with statistics on industrial hygiene and industrial safety.

Statistics are facts expressed in figures; and if the figures represent cost data, they are in a form of expression with which the industrialist is familiar.

If our committees could secure such data from a few of our large railroads and industries which have good medical departments, they would be of considerable value and might serve to establish a precedent for continued procedure by Industry.

It would be very helpful also if we could have a report on the relation of malaria to industry, prepared jointly by some group representing Industry, comparable to the report on Malaria Control for Engineers.

The minimum personnel requirements for a State Board of Health malaria control program are:

(a) An experienced malariologist;
(b) Technicians skilled in the identification of malaria plasmodia;
(c) An engineer trained and experienced in all forms of mosquito control, with some knowledge of entomology;
(d) An entomologist especially trained in mosquito identification and familiar with the ecology and bionomics of mosquitoes, particularly the Anopheline group.

These are essential minima. Each will need assistants, technical and clerical, if the program is to be an important one.

There seems to be a fairly general agreement as to the kind of workers needed for a well developed malaria control program. There are more differences of opinion as to methods of organization and administration.

One widely used method is to group all malaria control activities and personnel into one unit. This is a good plan, and some states have done excellent work with such an organization.

Another type of organization—which I consider much better—is one in which the grouping of personnel is based on the idea of bringing closely together in working units those with the same kind of special knowledge, skills and facilities; and not on the organization of a number of teams, or units, organized for special objectives and including various sorts of specialists. Or, to put it in another way, the preferred form is an organization in which those activities dealing directly with individuals, such as medical and nursing services, clinics, epidemiology, etc., are grouped into one division; those

dealing with things and the environments, such as engineering, sanitation, entomology, etc., in another; laboratories in another; business and finance in another, and so on. This is more like the successful type of organization of big business.

It may very probably be true that—considering a single objective, malaria control, by itself—the first form of organization would be more effective for a short time. However, the other arrangement is, I think, better, considering the public health program as a whole; and it is likely, in the long run, to produce greater results in any one objective.

Such an arrangement affords a greater degree of flexibility to the entire health program, and provides for closer cooperation and more productive effort on the part of specialists with similar training. It avoids administrative difficulties and complexities which inevitably come from the development of autonomous units to deal with a number of special activities, e.g., malaria control, industrial hygiene, typhus control, and others, which all require the team work of a similar group of specialists.

Also it will tend to minimize the competition between heavily subsidized special programs for the attention and time of local health departments.

Of course the administrative organization should provide for close cooperation and effective liaison between the different divisions, such as the cooperation between epidemiologist and sanitary engineer which has brought about such a considerable reduction in typhoid fever and other water and milk borne diseases.

It would be impracticable to include in a special malaria control unit *all* the different kinds of personnel needed for a complete malaria control program which would develop all potentially profitable activities.

The major essential items of a state plan for malaria control are:—(1) statistical and field studies to determine the location and relative importance of endemic foci of malaria and Anopheline breeding areas; (2) epidemiological and engineering plans for control; (3) promotion of projects for mosquito-proofing buildings, and for elimination of control of Anopheline breeding areas by private and governmental agencies; (4) developing cooperation with private and governmental agencies to avoid the creation of Anopheline breeding areas; (5) a general educational program to secure public and financial support.

The details of the program will, of course vary, depending on local conditions and available personnel and funds; but whatever

may be the form of administrative organization at the state level and the scope of the campaign, the actual control measures in the field will very likely be applied in an area with a full time local health organization. Every effort should be made to provide that, as far as possible, malaria control work be carried on as a component part of the routine activities of the local health organization with the help of the State organization, and not the other way around.

Many workers have pointed out from time to time that, although there is much to learn about malaria, we already have more information than we are using to control the disease. One of the most recent authoritative expressions on this point is in the 1941 Annual Report of the International Health Division of the Rockefeller Foundation:—

> "The main obstacles in the way of malaria control today are not so much technical or biological as they are social. They appear to consist of such lacunae as (1) fundamental absence of educated and effective public opinion; (2) too limited use of sound administrative principles in public health; (3) lack of sufficient numbers of trained personnel; (4) failure among officials to recognize economic phases of malaria and malaria control; (5) inadequate knowledge of methods for applying practically the results of research."

More consideration must be given to such items as these, in addition to the technical phases, if accelerated and sustained progress is to be made on malaria control.

All of our State Boards of Health have educational programs. More stress should be placed on public education in the need for malaria control and on control measures. Much has been done along this line; but one is sometimes dismayed to find a surprising lack of knowledge of malaria in some places. Several years ago, during a conference with the head of a very large and important federal agency—an engineer, by the way— I outlined some of the things they should do to stop the creation of malaria hazards, and he remarked with a note of surprise "Why, those things are practical".

On the train coming home from our last meeting, I met a friend who is the Dean of the College of Engineering in a Southern University. He was returning from a conference on education and we compared notes about our meetings. He was much interested in comments about the relation of engineering to the malaria problems of the South because, he said, he knew malaria made people sick but did not know that it ever killed anybody. Much more educational work is needed.

One of the amendments to the by-laws adopted at our last meeting relates to essay contests and provides that, on petition of ten members in any state, the president is authorized to appoint a committee to sponsor an essay contest among school children and to draw rules for such contests. Not a single petition has been received during the past year. It is suggested that a committee be appointed to make plans and rules for such essay contests and to promote contests in the various states.

Since one of the duties assigned to the Committee on Malaria Prevention Activities is "to study the relation of malaria to general health problems and administration . . .", consideration of the second item on the list of obstacles is within the committee's province. A special study and report on this topic would be very helpful to all of us engaged in administering control programs.

We are hopeful that the knowledge and skill acquired during the present emergency, and the large group being trained by actual experience in this current program, will help to fill, to some extent at least, the gaps listed as item (3) and (5).

The essential need for the conservation of man-power is bringing into sharp focus the absolute need of prevention of all sorts of illness and accidents, and we may be able in this emergency to awaken officials to the high cost of malaria.

REFERENCES

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2–A Brief Review of Needed Research in Malaria–*Public Health Reports,* Vol. 55, No. 40, October 4, 1940.

3–Malaria Control for Engineers. Report of the joint committee of the National Malaria Committee through its sub-committee on Engineering and the Sanitary Engineering Division, American Society of Civil Engineers. Proc. American Society of Civil Engineers, February, 1939.

4–Malaria Control–A report to the President, St. Louis Southwestern Railway Lines. Published by the St. L. S. W. Railway Lines (1921).

5–Craig, C. F. and Faust, E. C. Clinical Parasitology, 3rd Edition. Lea and Febigee, Philadelphia, Pa. (1943).

THE NATIONAL MALARIA SOCIETY

A Sketch

Mark F. Boyd

The National Malaria Society is a continuation of the organization formerly known as the National Malaria Committee, the change in name being effected in 1941 in the interests of consistency. Consequently any sketch of the history of the Society will largely deal with its evolution from the Committee.

Any organization which has existed for more than a quarter of a century may be expected to have undergone considerable evolution during such a period. Although its present pattern may be different from that set by its founders, its survival implies growth, and that it at least reasonably supplies a need felt by those who support it. In any event, then as well as now, it probably exercised its greatest usefulness as a forum for the exchange and dissemination of information relating to malaria and its control.

The Second Pan-American Scientific Congress held in Washington, D. C., adopted, on January 7, 1916, the following as its 19th resolution:

"That all American countries inaugurate a well-considered plan of malaria eradication and control based upon the recognition of the principles that the disease is preventable to a much greater degree than has thus far been achieved, and that the education of the public in the elementary facts of Malaria is of the first order of importance to the country's concern."

The proponent of this resolution, Dr. Frederick L. Hoffman, undertook to place these recommendations in operation, insofar as the United States was concerned. Through his initiative, plans were laid for a conference in Washington, in May 1916, during the sessions of the Congress of American Physicians, and Surgeon General Rupert Blue of the U. S. Public Health Service extended invitations to a group of 30 distinguished physicians, sanitarians and scientists to assemble for this purpose on May 10th. Those actually in attendance were Doctors C. C. Bass, Rupert Blue, H. R. Carter, E. S. Crum, Seale Harris, J. W. Kerr, M. J. Rosenau, E. R. Stitt, John M. Swan, W. G. Thayer, Robert Wilson, Jr., T. J. Headlee and L. O. Howard.

After deliberation it was decided that a National Committee on Malaria be formed, and a simple plan of organization was adopted. Although a restricted and selected membership was originally contemplated, this idea was practically ignored on organization and ac-

tually abandoned in the course of time. Annual dues were not required, and annual and special meetings were to be held on call of the chairman. It was decided that the objects of the organization should be (a) to stimulate interest in malaria problems; (b) to serve as a medium through which societies and individuals may become identified with the study and prevention of the disease; and (c) to coordinate the efforts of these agencies with constituted federal, state and local authorities. It was contemplated that these objectives could be achieved through the operation of sub-committees, eligibility to which would not require membership on the parent committee. The programs of the state organization which have so successfully dealt with these problems during the last two decades, must in part, at least, be credited to the enlightening influence of the committee. Surgeon General Gorgas, M. C., U. S. A., was elected Honorary Chairman, and Surgeon General Rupert Blue, U. S. Public Health Service, Acting Chairman, while Dr. Seale Harris, then Secretary of the Southern Medical Association, was elected secretary.

The Comittee was actually organized with 29 "charter" members, whose names are as follows:

Dr. C. C. Bass, Tulane Medical School, New Orleans, La.
Dr. Rupert Blue, Surgeon General, U. S. Public Health Service, Washington, D. C.
Dr. W. E. Britton, State Entomologist, New Haven, Conn.
Dr. H. R. Carter, Ass't Surgeon General, U. S. Public Health Service, Baltimore, Md.
Dr. C. F. Craig, Capt., M. C., U. S. A., Fort Leavenworth, Kansas.
Dr. W. H. Deaderick, Hot Springs, Arkansas.
Dr. W. E. Deeks, United Fruit Company, New York City.
Dr. Oscar Dowling, State Board of Health, New Orleans, La.
Dr. R. H. von Ezdorf, U. S. Public Health Service, New Orleans, La.
Dr. W. E. Gorgas, Surgeon General, U. S. A., Washington, D. C.
Dr. Frederick R. Green, Am. Med. Ass'n, Chicago, Ill.
Dr. Seale Harris, Secretary, Southern Medical Ass'n, Birmingham, Ala.
Dr. T. J. Headlee, State Entomologist, New Brunswick, N. J.
Dr. Graham E. Henson, Jacksonville, Florida.
Dr. Frederick L. Hoffman, Prudential Insurance Co., Newark, N. J.
Dr. L. O. Howard, Bureau of Entomology, Washington, D. C.

Mr. Arthur Hunter, New York Life Insurance Co., New York City.

Dr. W. D. Hunter, Bureau of Entomology, Washington, D. C.

Dr. J. W. Kerr, Ass't Surgeon General, U. S. Public Health Service, Washington, D. C.

Dr. W. S. Leathers, State Board of Health, University, Miss.

Mr. J. A. LePrince, U. S. Public Health Service, New Orleans, La.

Lieut. Col. Charles F. Mason, M. C., U. S. A., Balboa Heights, Canal Zone.

Dr. Joseph Y. Porter, State Board of Health, Jacksonville, Fla.

Dr. W. S. Rankin, State Board of Health, Raleigh, N. C.

Dr. M. J. Rosenau, Harvard Medical School, Boston, Mass.

Dr. E. R. Stitt, Medical Inspector, U. S. N., Naval Medical School, Washington D. C.

Dr. J. M. Swan, President, American Society of Tropical Medicine, Rochester, N. Y.

Dr. W. S. Thayer, John Hopkins Hospital, Baltimore, Md.

Dr. Robert Wilson, Jr., President, Southern Medical Ass'n, Charleston, S. C.

Although some consideration had been given to a meeting of the committee during the period of the 1916 sessions of the Southern Medical Association in Atlanta, Georgia, from November 13-16, this did not materialize. Dr. Frederick L. Hoffman however did deliver before a joint session of the sections on Medicine and Public Health of that association on the 16th, an address entitled "A Plea and a Plan for the Eradication of Malaria", which elaborted on the projected organization.

At a called executive meeting of the committee held on June 6, 1917 at the Biltmore Hotel, in New York City, it was decided that the first general meeting of the committee would be held in conjunction with the next meeting of the Southern Medical Association, to be held in Memphis, Tennessee, from November 12-15, 1917.

As a result a meeting of the committee was scheduled for Monday, November 12th, and it was decided that at this time all consideration of malaria by other sections of the Southern Medical Association would be relegated to this meeting. Prior to the Memphis meeting, Dr. Seale Harris withdrew from the secretaryship, and Assistant Surgeon General H. R. Carter, U. S. Public Health Service was appointed to the office by chairman Rupert Blue.

The Memphis meeting was held as scheduled on November 12th, at the Hotel Chisca, the scientific program occupying the entire

day. Due to the absence of the Honorary and Acting Chairman, Dr. Carter presided. At an adjourned business session held the following day, it was decided to have the proceedings of the meeting published in permanent form, and the future meetings be held in conjunction with those of the Southern Medical Association.

The influenza epidemic caused the cancellation of plans for the meeting of the Southern Medical Association in 1918 and of the committee as well. The committee was quiescent until a called executive meeting was held on June 5, 1919, in the office of the Surgeon General of the Public Health Service, and plans were laid for resumption of meeting with the Southern Medical Association.

The annual meetings of the Southern Medical Association were resumed in 1919 with the Asheville, N. C. session, at which, and for several years thereafter, the committee meeting was regarded by the Southern Medical Association as the Malaria Division or Symposium of the Section on Public Health.

It was soon recognized that these joint meetings with the Southern Medical Association offered distinct advantages to the committee. The association represents that region of the United States where malaria constitutes an outstanding problem, a problem to which the association was acutely alert. This active interest of the Southern Medical Association in the malaria problem was expressed by the formation of a malaria commission by the association as early as 1912, which was authorized at the Hattiesburg meeting in 1911, and the segregation of the malaria papers which appeared on its program in a special symposium in its Journal as early as 1914. Upon organization of the committee, the Southern Medical Association allowed its malaria commission to lapse. The cordial and continued welcome of the association's officers to the committee, their helpful counsel and material assistance in program space, meeting places and publication outlet through their Journal, cemented a relationship that has endured and remains pleasant and harmonious. The Society owes, and is pleased to acknowledge with gratitude, its indebtedness and obligations to the Southern Medical Association.

Dr. Seale Harris withdrew as secretary on the termination of the organizational period. He was succeeded by Dr. H. R. Carter, then in charge of the program of field investigations of malaria, of the Public Health Service, who continued as secretary until transferred to other duties in 1920. His successor as director of the service's program, Dr. L. D. Fricks, was named acting secretary, an office to which he was elected at the Louisville meeting in 1920,

and continued therein until 1926. He in turn was transferred to other duties and succeeded by Dr. L. L. Williams, Jr., assigned to take charge of the malaria program of the service. Dr. Williams was elected secretary at the Memphis meeting in 1927 and occupied the office until 1929. He in turn was succeeded by Dr. Mark F. Boyd who is the present Secretary. The places at which the annual meetings have been held are shown in the accompanying table, together with the names of the principal current officers:

ANNUAL MEETINGS

	Year	*Dates*	*Place*	*Chairman*	*Secretary*
	1916	May 10	Washington, D. C.		Seale Harris
	1916	Nov.	Atlanta, Ga.	Surg. Gen. R. Blue	H. R. Carter
	1917	June 6	New York City		
1st	1917	Nov. 12-13	Memphis, Tenn.	Surg. Gen. R. Blue	H. R. Carter
	1918	No meeting of Southern Medical Ass'n because of influenza epidemic			
	1919	June 5	Asheville, N. C.	Surg. Gen. R. Blue	H. R. Carter
2nd	1919	Nov. 10	Asheville, N. C.	Surg. Gen. R. Blue	H. R. Carter
3rd	1920	Nov. 15	Louisville, Ky.	Surg. Gen. R. Blue	L. D. Fricks
4th	1921	Nov. 14-17	Hot Springs, Ark.	Dr. W. S. Leathers	L. D. Fricks
5th	1922	Nov. 14-16	Chattanooga, Tenn.	Dr. W. S. Leathers	L. D. Fricks
6th	1923	Nov. 12-13	Washington, D. C.	Dr. S. W. Welch	L. D. Fricks
7th	1924	Nov. 24	New Orleans, La.	Dr. J. A. Ferrell	L. D. Fricks
8th	1925	Nov. 10-12	Dallas, Texas	Dr. W. E. Deeks	L. D. Fricks
9th	1926	Nov. 17-18	Atlanta, Ga.	Dr. J. A. Hayne	L. D. Fricks
10th	1927	Nov. 16	Memphis, Tenn.	Dr. V. G. Heiser	L. L. Williams, Jr.
11th	1928	Nov. 12-15	Asheville, N. C.	Dr. F. J. Underwood	L. L. Williams, Jr.
12th	1929	Nov. 21-22	Miami, Fla.	Dr. Wm. Krauss	L. L. Williams, Jr.
*13th	1930	Nov. 11-14	Louisville, Ky.	Mr. J. A. LePrince	Mark F. Boyd
14th	1931	Nov. 18-20	New Orleans, La.	Dr. S. S. Cook	Mark F. Boyd
15th	1932	Nov. 15-18	Birmingham, Ala.	Dr. E. L. Bishop	Mark F. Boyd
16th	1933	Nov. 14-17	Richmond, Va.	Dr. C. F. Craig	Mark F. Boyd
17th	1934	Nov. 13-16	San Antonio, Tex.	Dr. Henry Hanson	Mark F. Boyd
†18th	1935	Nov. 19-22	St. Louis, Mo.	Dr. L. L. Williams	Mark F. Boyd
19th	1936	Nov. 17-20	Baltimore, Md.	Dr. H. C. Clark	Mark F. Boyd
20th	1937	Dec. 1-3	New Orleans, La.	Dr. W. V. King	Mark F. Boyd
21st	1938	Nov. 16-18	Oklahoma City, Okla.	Dr. T. H. D. Griffitts	Mark F. Boyd
x22nd	1939	Nov. 22-24	Memphis, Tenn.	Mr.L. M. Clarkson	Mark F. Boyd
z23rd	1940	Nov. 13-15	Louisville, Ky.	Mr. W. G. Stromquist	Mark F. Boyd
s24th	1941	Nov. 11-13	St. Louis, Mo.	Dr. J. N. Baker	Mark F. Boyd
**25th	1942	Nov. 10-12	Richmond, Va.	Mr. J. H. O'Neill President	Mark F. Boyd

*Adoption present constitution and by-laws annual dues set at $1.00.
†Committee first defray cost of symposium reprints. Annual dues set at $2.00.
xJoint publication of "Syllabus."
zAffiliation with American Ass'n for the Advancement of Science, January 22.
sAmendments to constitution including change of name to Nat'l Malaria Society annual dues set at $3.00.
**Appearance of Volume I of the Journal of National Malaria Society.

The number of sessions held during the annual meetings has been variable. Prior to 1922 all sessions were held on one day, but beginning with that year the Southern Medical Association began to stagger the sectional meetings, and to 1929, half day sessions were held on two days. Beginning with 1930, an additional half

day was added for a business session, so that subsequent to that year, excepting 1936 and 1942, sessions have been held on three half days. Two half day sessions have been invariably devoted to the consideration of scientific papers. The number of these has varied from 3 in 1922 to 18 in 1842, and since 1930 there have not been less than 11 at any meeting. The demand for space on the programs justifies an additional scientific session.

Of recent years the American Society of Tropical Medicine has been meeting conjointly with the Southern Medical Association, and since 1931 one scientific session of the National Malaria Society has been held jointly with the American Society of Tropical Medicine. Since 1941 the other scientific session has been held jointly with the Sanitary Engineering group of the Southern Branch of the American Public Health Association. In general medical and epidemiological papers have been assigned to the session held jointly with the American Society of Tropical Medicine, and entomological and engineering papers to the session held with the American Public Health Association. At the 1942 Richmond meeting, it was decided that the annual meetings should consist of three sessions, not more than two of which shall be held jointly with other organizations. As already mentioned the Southern Medical Association had been focusing attention on the malaria problem in the south, as far back as 1913, and in that year the section on medicine held a "Symposium on Malaria," the papers of which appeared under that designation in a special issue of the Journal in 1914. The editors of the Southern Medical Journal revived this practice in 1922, when the papers presented before the committee at Hot Springs in 1921 were published as a Symposium. The papers from the committee's program, including sub-committee reports, or a selection thereof, plus occasional malaria papers contributed to other sections, were annually thereafter published as a group, in one, or at times several, issues of the Journal, until 1941. From 1925 to 1929 a subvention of the Rockefeller Foundation provided for the purchase of sufficient reprints of the symposia for distribution to members and others. On the discontinuance of this assistance the management of the Southern Medical Association generously donated sufficient reprints of the symposia for distribution to the membership of the committee, and continued the courtesy until 1933. Financial stringency during 1934 did not permit of the reprinting of the symposium for 1933. Subsequently to that year however, and until 1941, the committee purchased the reprints from its own funds.

Prior to the 1930 meeting at Louisville, it was becoming apparent that the current procedure for election to, and continuation

in membership, had resulted in the accumulation of an uncertain number of individuals whose interest in the organization had flagged, since they did not attend or participate in the meetings, and the distribution of mail and publications to them was a source of unjustified expense. It was furthermore evident that for other reasons a real need existed for more definite organization. Consequently there was submitted a constitution and set of by-laws which had been drafted by a special committee, which was adopted at the Louisville meeting. Among other things this provided for annual dues of one dollar per annum to provide funds for operating expenses, and the automatic dropping of members who became 2 years in arrears in their dues. The beneficial results were soon apparent. When it became evident that the committee should no longer accept the symposium reprints gratis from the Southern Medical Association, the dues were raised to $2.00 in 1935.

Among the accomplishments of the committee may be mentioned the publication of the teaching syllabus "Malaria Control for Engineers," which was first mimeographed by the U. S. Public Health Service and became in such demand that it was published in the Proceedings of the American Society of Civil Engineers for 1939, and in reprint form widely distributed for class room instruction. This was the fruit of a joint enterprise of the Subcommittee on Engineering of the Committee, and a committee of the Sanitary Engineering Division of the American Society of Civil Engineers. In 1940 the Committee became affiliated with the American Association for the Advancement of Science. Mention should also be made that the Committee was one of the organizations sponsoring the "Symposium on Human Malaria" which featured the 1941 meeting of Section N of the American Association for the Advancement of Science at Philadelphia. A large proportion of the Contributions were by committee members.

It was becoming increasingly evident that the actual status of the organization was incorrectly expressed by the designation "committee," and that in all justice to the Southern Medical Association, should no longer permit that organization to continue to bear even a part of the financial load of its publication expenses. The matter had been carefully considered by a special subcommittee which recommended certain constitutional changes at the 1940 meeting in Louisville. These were adopted a year later at St. Louis. Among the innovations the name of the organization was changed to the National Malaria Society, annual dues were set at $3.00, two-thirds of which are to be transferred to a publication fund, an editorial board created, and the publication of a journal authorized.

The Journal, presenting the papers presented at the 1941 meeting in St. Louis, was introduced to the membership at the Richmond meeting in 1942. This initial volume (Vol. I) appeared as an annual. The editorial board expects to publish Vol. II during 1943 as a semi-annual, and establish it as a quarterly at an early date. At present it serves to publish the proceedings of the meeting, but when on a quarterly basis the editor will be prepared to accept suitable contributed papers. The financial side of the publication program is sound, while funds are adequate for the modest program.

With a gradually enlarging membership the Committee became more democratic, and the original concept of a restricted and selected membership was forgotten.

At the time of the adoption of the 1930 constitution, the roster contained the names of 15 honorary members and 156 active members. At the time of the 1942 meeting in Richmond, there were 19 honorary and 189 active members. It is expected that the publication of the Journal will do much to both stabilize and enlarge the membership.

The present purposes and functions of the Society, as expressed in the constitution, are "to study malaria and stimulate scientific and practical interest among individuals and organizations, in its cause, prevalence, prevention and treatment." Any person who has shown scientific or practical interest in malaria problems is eligible for active membership. Further information may be secured from the current secretary, Dr. Mark F. Boyd, P. O. Box 997, Tallahassee, Florida.

At the 1942 meeting in Richmond, the Society authorized the appointment of a committee consisting of a physician, a sanitary engineer and an entomologist, to cooperate with the Army, the Navy and the Public Health Service, on request, and to make available to them the technical skill and knowledge possessed by the members of the Society. With this authority, the current president, Brigadier General J. S. Simmons, M.C., U.S.A., selected Dr. H.C.Clark, Mr. J. H. O'Neill and Dr. F. C. Bishopp to compose the committee. It was also determined that in the event the Southern Medical Association does not meet in 1943, the question of a session will be settled by the president, Brigadier General Simmons.

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VARIATIONS IN THE ASEXUAL CYCLE OF PLASMODIUM WHEN TRANSFERRED TO AN ABNORMAL HOST*

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From the biological point of view it is just as important to know what changes are produced on the parasite by the host as it is to know the effect of the parasite on the host. This side of parasitology seems to have been somewhat neglected for the more obvious pathogenic effects produced by parasitism. In the field of malaria the changes occurring in the parasite as a result of a change in host are just beginning to be studied. In recent years the female canary has lost its place as the only experimental host of avian plasmodium. Wolfson (1938) has found that young ducks are susceptible to certain species of *Plasmodium*. Coggeshall (1938) isolated a species of plasmodium (*P. lophurae*) in the pheasant which is infective for young chickens. *P. lophurae*, according to Wolfson (1941), kills young ducks but produces a very mild infection in canaries. Brumpt (1935) isolated a new species, *P. gallinaceum*, from a chicken and found that this species is invariably fatal to young chicks, but assumes a chronic condition in adult fowls. It is infective for some species of birds, but not for others. Coatney (1938) isolated a strain of *P. relictum* from a young pigeon and succeeded in establishing it in adult pigeons. He found it to be only mildly infective for canaries. It has since been found to produce high infections in the latter host.

Young ducks about 3 days old, and day-old chicks, have been found to be susceptible to several species of avian malaria, normally infective for canaries. Wolfson (1938) infected young ducks with a strain of *P. cathmerium* and found that the sporulation period came later in the evening than in infections of the same species in canaries. Hegner and West (1941a and 1941b) found the asexual cycle in ducks to be 24 hours in length but the degree of synchronicity was less, and sporulation occurred 3 to 4 hours later. In day-old chicks the asexual cycle was lengthened to 48 hours and sporulation occurred in the morning instead of late afternoon. The number of merozoites produced per segmenter was much smaller in chicks than in ducks or canaries. Slight morphological variations were ob-

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served, especially in the gametocytes. Wolfson (1940) suggests that the synchronicity may be increased in duck embryos.

The only strain of *P. relictum* studied in abnormal hosts appears to be the matinal strain (Wolfson, 1939). The asexual cycle evidently was not altered though the infections were so low as to make a thorough study difficult. A large percentage of the gametocytes appeared to be of the elongate type in the duck, but assumed the round form when again transferred back into the canary. The presence of the exoerythrocytic stages may be dependent on the species of host (Wolfson, 1941).

In the present studies the pigeon strain of *P. relictum* was used. This strain has been designated as the 1 P strain of *P. relictum* by the committee on terminology of strains of avian malaria (Huff, Boyd, and Manwell, 1942). Adult pigeons and canaries kept in screened cages were used as hosts. Inoculations were intravenous. The results were obtained from blood smears made at intervals of 2 hours and stained with MacNeal's tetrachrome stain. In the canary the infections appear to be as pathogenic as in the pigeon. High parasite numbers are frequently found and occasionally the infection is fatal. The parasites have been carried in canaries for more than 12 months without allowing the infection to become latent. When transferred from canaries to pigeons or from pigeons to canaries the first 2 or 3 infections are generally low. After this the degree of the infection appears to be fairly uniform. The most outstanding variation noted when the infection is transferred to the canary is in the asexual cycle.

In making the counts to determine the time of segmentation the parasites were placed in one of three groups depending on the number of nuclei contained in each parasite. The groups were separated as follows: those containing 1 to 4 nuclei, those containing 5 to 8 nuclei, and those containing 9 or more nuclei. Since merozoite counts have shown the number produced by each segmenter to be relatively small the group containing 5 to 8 nuclei was considered to be the most representative. Since some parasites produce more than eight merozoites, the actual peak of sporulation may be somewhat later than that time at which the greatest number of parasites have 5 to 8 nuclei.

The asexual cycle in the pigeon has been studied by Coatney (1940). The synchronicity is high, as only an occasional segmenter is found in the interval between the peaks. The time between successive sporulations was found to be 27 hours. Since the synchronicity and periodicity have been thoroughly studied, the cycles in only

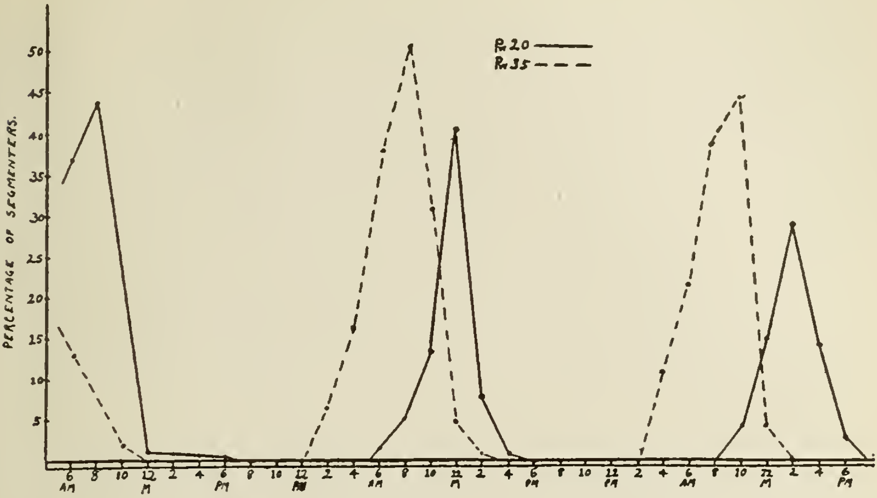

FIGURE 1.

a few pigeons were observed. Figure 1 shows that these correspond to the observations of Coatney (1940).

When the asexual cycle of the 1 P strain is studied in successive infections in the canary, it is found that the synchronicity may be slightly increased and that the period of sporulation occurs approximately every 24 hours falling between 8 and 10 o'clock in the morning.

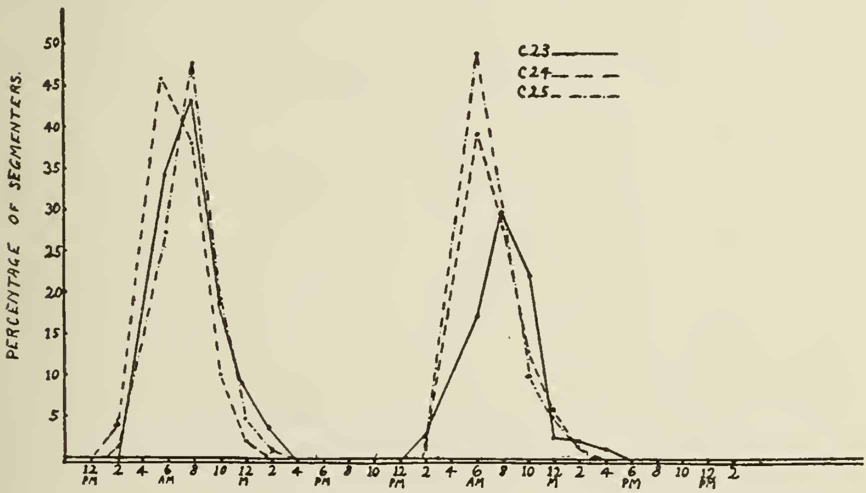

FIGURE 2.

These results are shown in Figure 2. From about 4:00 P. M. to 2:00 A. M. there are no parasites containing more than 4 nuclei. Parasites having 5 to 8 nuclei begin to appear and the number increases until approximately 8:00 A. M. The counts show (not

on the figure) that with only two exceptions the number having 9 or more nuclei occurs at 10:00 A. M. This indicates that the peak of sporulation falls somewhere between 8:00 A. M. and 10:00 A.M. daily. The average length of the asexual cycle for all birds studied using these groupings of parasites was 23.53 hours.

Previous to the inoculations into the three birds, No. C23, C24, and C25 the parasites had been passed through 23 canaries successively. The time interval since the initial inoculation into the canary from the pigeon was 193 days. Another group of three canaries, No. C59, C60, and C61 were studied after the infection had been carried through 37 canaries over a period of 352 days. The results on these birds correspond with those of the 3 birds shown in Figure 2.

The only morphological differences so far noted when the 1 P strain is studied in the two hosts are found in a slight variation in the number of merozoites produced per segmenter. In the pigeon the average number is 8.54; the extremes being 6 to 14. In the canary the average is 9.15; the extremes being 6 to 16. The average difference of .61 is not very significant.

The percentage of gametocytes and the ratio of microgametocytes to macrogametocytes has been determined in several canaries and pigeons but these have been found to be so variable especially in the pigeon that no consistent conclusions can be reached as to the relationship in the two hosts.

In addition to being another instance of a study of transfer of malaria parasites to a different host the present work is the only record where the same parasite species has been studied in two susceptible adult hosts in both of which a more or less typical infection results. The results of studies in both day old chicks and young (2 or 3 day old) ducks may be influenced by the age resistance that later develops. There is no age resistance active in either pigeons or canaries to the 1 P strain. The infections with this strain produce comparable immune reactions to superinfection in both hosts. Since no other strain produces an infection in the pigeon, no comparison can be made of the cross immunity with other strains of *P. relictum* and with other species of *Plasmodium* in this host. However, cross immunity has been studied in the canary. It was found that various strains of *P. relictum* and *P. cathemerium* produce an effective immunity to the 1 P strain but that the reciprocal crosses showed very little immunity. Not only can much information be obtained on the immune mechanism by a comparison of the reactions of one strain in two or more different hosts but also the question of strains and variations under differing conditions may be cleared up.

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REVIEW OF RECENT RESEARCH ON DRUG PROPHYLAXIS AND TREATMENT OF MALARIA

(A Report to the National Malaria Society)

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This review was prepared at the request of the Committee on Medical Research and the period covered is from September, 1941 to September, 1942. It includes only the examination of the literature available in Panama and attention must be called to the fact that the present emergency has greatly reduced the number of articles published on the subject. Priorities on supplies and shipment also limit the receipt of records. At the close of the war we shall, no doubt, be flooded with reports on the management of malaria. More investigations in chemotherapy are certainly indicated and this war may provide some new approaches to the problem.

The United States Public Health Reports (1) calls attention to the compelling necessity for increasing knowledge of the prophylaxis and treatment of malaria. Molitor (2) states that we seem justified at present in limiting discussions of effective antimalarials to the quinine, plasmochin and atabrine group but that the ideal antimalarial still has to be found. Up to date only the synthetic compounds belonging to the sulfanilamide group have offered some promise. He calls attention to the fact that almost none of the hundreds of alkaloids and glucosides isolated from tropical plants has been subjected to a pharmacological analysis which today could be regarded as adequate. It may therefore be justified to expect unforeseen and valuable results from a thorough investigation of this field.

The British Army (3) fully realizes that cases of malaria may be expected in men who return from service overseas in malarious countries and that a high proportion of those seen have been suffering from the dangerous malignant tertian variety. They use a standard treatment as follows:

Days 1 and 2:—

Quinine bisulphate or quinine hydrochloride, grains 10 in solution, in one fluid ounce of water, by mouth, three times in 24 hours.

Days 3, 4, 5, 6 and 7:—

Mepacrine hydrochloride, 0.1 gramme tablet, three times a day, swallowed whole with a draught of water, after food.

Days 8 and 9:—

No antimalarial drug treatment.

Days 10, 11, 12, 13 and 14:—

Pamaquin, 0.01 gramme tablet, three times a day, after food.

Mepacrine is the British equivalent of atabrine, Pamaquin that of plasmoquine.

Dauncey (4) advocates the intramuscular injection of quinine in the treatment of malaria. The site for the injection that he selects is the upper part of the middle third of the outer aspect of the thigh; here one can feel the needle pierce the fascia lata. The most effective time to give the treatment is from one hour to half an hour before the temperature begins to rise. His aim is to get the maximum concentration of quinine in the blood while the merozoites are scattered in the blood stream. He believes that one well timed injection of five grains of quinine is sufficient to cure the acute symptoms. By this form of treatment a large amount of quinine can be saved and the patient spared a long course of unpleasant treatment.

The annual report of the Federated Malay States continues to show a preference for quinine over the new drugs that have been given a trial.

In southern parts of China (6) the root-bark of an indigenous tree has been used for the past thirty years to prepare an antimalarial drug. The scientific name given the three is *Fraxinus malacophylla* Hemsley. For convenience the tree has been called the sinine tree. The drug sinine is said to be just as good as quinine for all kinds of malaria. A four days course of treatment is said to kill all parasites. Very little is known about the drug but the tree is abundant and widely distributed. The chunine tree of the same region is also said to produce a similar useful drug (chunine).

Condorelli (7) reports an interesting case of purpura haemorrhagica in a case of malaria under treatment with quinine. A man aged 27 was serving in Abyssinia in 1935. For a time he was on prophylactic quinine daily and showed no sign of intolerance to the drug. In spite of his routine prophylaxis he fell ill with malaria. The attack was not severe but it was accompanied by profuse epistaxis and a generalized petechial rash. He made a rapid recovery under other treatment. In 1936 he returned to Italy and in 1939 he again fell ill with malaria. It was a sharp attack. There was no haemorrhagic phenomena until two days later when he was given an injection of 1 gm. of quinine. Half an hour after this treatment profuse epistaxis, bleeding from the guns, a diffuse petechial rash all over the body, intense subconjunctival haemorrhage in both eyes, intense haematuria, and a large haematoma at the site of the injection. He was dangerously ill but eventually recovered. Later he was given an experimental injection of 0.5 gm. of quinine and the haemorrhagic

phenomena again appeared together with a rise in temperature. A month later a similar dose of quinine caused a slight rise of temperature but no haemorrhagic symptoms. Four and a half months later quinine caused a slight chill but no haemorrhagic symptoms.

Lamprell (8) states that atebrin lowered the incidence of clinical malaria to a greater extent than did quinine. Atebrin in addition had the great practical advantage of being popular with the people whether as treatment for an attack or for prophylaxis. The expenditure on atebrin was about seven times as great as on quinine.

Rose (9) advocates a daily prophylactic dose of 0.06 gm. of atabrine and has had tablets of this prepared. He is not prepared at this time to give definite figures of the results obtained.

A report (10) from the Federated Malay States includes eighty cases that were treated with "Prontosil album," a proprietary sulphanilamide. The series contained the following infections: *P. falciparum* 34, *P. vivax* 38 and *P. malariae* 8. The dosage was 3.0 grm. daily, given in two doses of 1.5 grm. Results were controlled by treating a parallel series of sixty-eight cases with quinine bihydrochloride given at 2.0 grm, a day for every hundred pounds of body weight. Mosquitoes fed on "crescent" carriers after seven day treatment with "Prontosil" were readily infected. It was concluded that: (I) Prontosil is not so efficient as quinine in acute *P. falciparum* malaria; (II) "Prontosil" is still less effective in acute *P. vivax* malaria; (III) "Prontosil" is not an effective gametocide either in *P. falciparum* or *P. vivax* malaria. The drug has no place in the practical treatment of malaria from its low efficiency and high cost.

Schwartz (11) reports the use of Sulfathiazole to terminate artificially induced malaria in nine patients. Relapses occured in 5 of these cases. The action of the drug is slower than that observed with quinine according to his experience.

De Leon (12) reports the intravenous use of Ambesid, a sulphanilamide preparation. In acute attacks of *P. falciparum* infections it is a good substitute for atebrin when intravenous treatment is indicated.

Coggeshall, Maier and Best (13) treated 17 patients suffering from malaria in Gorgas Hospital with promin and 13 with sulphadiazine. They conclude that there are no reasons for giving either drug in preference to quinine or atebrin for the treatment of malaria, but that both may be looked on as important substitutes.

Mapharside (14) is a trivalent arsenical preparation that has been used to some extent in therapeutic malaria. Niven reports its use on 20 *falciparum,* 9 *malariae* and 20 *vivax* infections using an equal control number in the *falciparum* and *vivax* infec-

tions treated with quinine. The mapharside treatment consisted in the administration of two intravenous injections, with an interval of from five to seven days, of 0.04 and 0.06 gm. respectively. He concludes that its use should be limited to the treatment of therapeutic *vivax* infections.

The Imperial Chemical Industries Limited (15) have synthesized a substance, pamaquin, which is believed to be identical with plasmoquine (Bayer). The biological tests confirm this view.

A description of thrombopenic purpura caused by chinin in a Chinese boy 17 years old has been recorded by Siegenbeek van Henkelom (16).

Thoroughman (17) reports the experiences of a hospital on the use of donors in Soochow, Kiangsu, China. Malaria is endemic in Soochow. The donors were for the most part coolies. One hundred and four patients gave no history of recent malaria and no parasites were found in their bloods. The blood films of the donors (coolies) were also negative, yet 45 of these 104 patients developed malaria within a period of 20 days following the transfusion. Twenty-five of the patients had *P. vivax* parasites and 12 *P. falciparum* parasites while the species were not determined in 8 patients. The attacks were easily controlled by quinine. There was no case among 34 patients who received prophylactic quinine for three days after transfusion.

Marks (18) reports an accidental quartan malaria infection in a two-months-old infant. This child received three intramuscular injections of whole blood while under treatment in a hospital in Miami, Florida. The donors of the blood were the father of the infant and a laboratory technician. Neither of the donors had any history of malaria nor did their blood films reveal any parasites. The mother also gave no history or findings of malaria. He concludes that the child had no opportunity to acquire malaria in the natural way and one of the donors was responsible for the accidental transmission.

Gordon (19) reports a case of malaria that was accidentally transmitted by a transfusion of stored blood. A boy of seven years received three transfusions of stored blood for the relief of anemia secondary to sepsis. Forty-four days after the first transfusion and 33 after the last, he developed recurrent fever. Quartan parasites were found in the blood films. The boy lived in a district where malaria was unknown. Two donors were involved. One never had been in a malarial region while the other, had lived in Italy and had a history of malarial attacks in the past. The Italian's blood revealed a

few quartan parasites. His blood had been stored only two days before being used for the transfusion. Gordon believes that a donor's blood should be stored for a period of not less than eight days before using it for transfusion. The general opinion is now held that such donors can be safely used for the production of serum and plasma.

Castelli (20) of the Military Hospital of Padua, offers such information on the question of relapse in soldiers from the Italian Campaign in Africa. Between January, 1937 and August, 1939 eighty-eight patients were admitted suffering from relapse of malaria acquired in the military service in East Africa. The author concludes that relapses are rare after 15 months from the date of infection, and exceptional after two years. *P.vivax* was responsible for a ten-fold greater number of these relapses than was *P. falciparum* though the latter had the highest incidence in primary cases in Africa. No patients were admitted during the period named with *P. malariae.*

Granett (21) gives results of comparative tests of established repellent substances and a recently developed proprietary synthetic organic chemical mixture containing diethylene glycol monobutyl ether acetate, diethylene glycol monoethyl ether, ethyl alcohol, corn oil and perfume. This was developed from tests of nearly 1000 compounds and mixtures. It is superior to citronella and 42 representative proprietary products in lasting power.

Russell and Knipe (22) record a second year's experience with a spray killing mosquito method. As in the former year's work they used 19 parts of kerosene and 1 part pyrocide 20. They used this spray outside of the houses under the eaves as well as inside the house and each house was treated in this manner twice a week. The amount of spraying mixture used was 0.3 litre per 10,000 cubic feet sprayed. The method is effective in greatly reducing malaria transmission and the cost is less than antimalarial work would be in the same area.

Investigations (23) were carried out in Moscow on the possibility of destroying Anophelines in buildings by the light mist or aerosol resulting from the evaporation of Anabasine by heat. One method of obtaining it was to pour a water solution of anabasine sulphate on to quick-lime. The correct proportion was found to be 1 part anabasine sulphate and 1 part water to 6 parts lime. The minimum concentration of anabasine in air that killed all Anophelines in 8 minutes was 0.2 oz. per 1,000 cu. ft. and the rate at which anabasine sulphate must be used to give this is 1-oz. per 1,000 cu. ft. It is said to be better and cheaper than hydrocyanic acid gas and is harmless to fowls, rabbits, food-stuffs and germinating seed.

The Gorgas Memorial Laboratory (24) has continued its observations in its Santa Rosa Station with the following changes in effect from September, 1941 to August, 1942:

1. No plasmochin simplex was used.
2. The quinine group received 18 grains of the sulphate tablets a day for five days. The dosage for children being reduced to suit age and size.
3. The atabrine group was treated with the Winthrop Chemical Company's Dihydrochloride tablets 0.1 gm. three times a day for five days.
4. Blood film surveys were conducted bimonthly instead of monthly although a medical inspection was made of each village in the months when no survey was conducted.
5. Two control areas were surveyed monthly and offered voluntary treatment with quinine without supervision. One of these controls was on the lake shore and the other in the hills 3 miles distant.

The Parasite Rates for the four Groups follow:

Groups in Experiment	Monthly or Bimonthly Ave. Rate	Cumulative for the Year
Quinine (6 surveys)	12.1	25.9
Atabrine (6 surveys)	15.4	32.2
Lake Shore control (12 surveys)	25.8	43.2
Hill village control (11 surveys)	7.4	19.9

From the months of April to and including August there were many returning inhabitants who had been employed for some months with labor forces constructing highways, etc. When these people left their homes they averaged 5 to 8 percent positive, when they returned the rate was 20 to 30 percent according to their home villages. This raised the rates above the old levels more than the reduction of the surveys to a bimonthly period. From a therapeutic viewpoint we still consider quinine and atabrine to be equally effective. The people will take atabrine in a voluntary manner much better than they do quinine. We can, however, treat 5 cases with quinine for the cost of 1 case with atabrine. There were 48 babies, from birth to 12 months, examined in these towns. Twenty-five in the treated towns and twenty-three in the control towns. None of the 48 babies were positive for malaria in the first 12 months of life. At eighteen months there were two positives. One in the atabrine

group and one in the control town. Most of our community malaria rates are due to chronic malaria and to relapse. It is still apparent that we need a good gametocide that can be safely given over long periods of time in the field by non-medical attendants.

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MALARIA MORTALITY AND MORBIDITY IN THE UNITED STATES FOR THE YEAR 1941*

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INTRODUCTION

Yearly reports on the status of malaria in the Southern United States beginning with 1930 have been compiled by the writer and presented before the National Malaria Society. The data have been generously furnished by state bureaus of vital statistics and have consisted primarily of deaths due to malaria, tabulated both by states and by counties. It has been possible by translating these data into rates per 100,000 population to follow the year-by-year malaria trends, including both the cyclic increases and declines throughout the entire area and the minor but not necessarily unimportant variations in counties or groups of counties. Samplings of the reported morbidity data for 1933 (Faust and Diboll, 1935) indicated that these were not to be depended on as criteria for malaria incidence. Beginning in 1935 malaria mortality data were obtained from certain other moderately malarious states and by 1939 all of the forty-eight states were cooperating.

As a result of an analysis of the information compiled it was possible to note the apparently cyclic peaks of malaria, in 1915, 1921, 1927-1928, and 1933-1934 (Dauer and Faust, 1936) and to predict that another peak was due in 1939 or 1940. Confirming the earlier report of Maxcy (1923) it was demonstrated that heavy areas of endemicity were located in (1) a triangular block of counties in South Carolina, Georgia, Florida and Alabama, (2) the Mississippi delta region from Cairo, Illinois to Natchez, Mississippi, (3) in the counties of Southwestern Arkansas, Northeastern Louisiana, Southeastern Oklahoma and Eastern Texas, and (4) in the counties of Texas near the mouth of the Rio Grande. Moreover, following peak years it became evident that a reduction in malaria deaths in highly malarious counties was not necessarily accompanied by a decrease in mortality in adjacent counties, which frequently had an increment. This suggested radiating dissemination of the disease.

While concrete proof has been relatively scanty, cumulative information indicates that malaria as a primary cause of death is due

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almost always if not invariably to infection with *Plasmodium falciparum*, whereas *Plasmodium vivax* to a very great extent and *P. malariae* incidentally contribute to malaria morbidity. Moreover, endemic malaria in the United States outside the Southern States is due almost without exception to *Plasmodium vivax;* cases of *P falciparum* in these areas are introduced and have not become established.

Presentation of 1941 *Data*

The present report is based on information received from all of the States and the District of Columbia, and includes both deaths and reported cases of malaria by states and political subdivisions. This information is summarized by states in Table 1. For the fourteen Southern States additional information is included, namely the mortality rates by states for each year from 1929 through 1941, together with the average rate for this block of states (Table 2, Fig. 1). Moreover, an examination has been made of the apparently actual and potentially dangerous malaria foci in 1941 and this information has been visualized in a spot map (Fig. 2).

Malaria mortality.—Twenty-six states and the District of Columbia had 1390 deaths due to malaria. Of these 1113 were reported from the fourteen Southern States and probably most of the remainder (277) were cases which had acquired infection outside of the states in which they died. The rate for the United States as a whole was 0.1055 per 100,000 population, while that for the fourteen Southern States was 2.73.

Eighty per cent of all deaths was reported from the fourteen malarious Southern States; by population this four-fifths of the total deaths occurred in 30 per cent of the total population. Nevertheless, in these Southern States, with one exception (Oklahoma), the rates were the lowest on the record and the average was definitely favorable. In Oklahoma the 1941 rate was 2.2, as contrasted with only 1.0 for 1940, but constituted a slight decline from the 1939 rate 2.5. However, the deaths for 1939 were reported from 23 counties, those for 1940 from 16 and those for 1941 from 26 counties, suggesting an increase in death-producing malaria territory. With reference to deaths by counties in other states, in Alabama there was a decrease of 6 counties reporting deaths (42 vs. 48); in Arkansas, a decrease of one county (50 vs. 51); in Florida, an increase of 3 counties (40 vs. 37); in Georgia, a decrease of 9 counties (46 vs. 55); in Kentucky, a decrease of one county (13 vs. 14); in Louisiana, a decrease of 2 counties (31 vs. 33); in Mississippi, a decrease of 13 counties (47 vs. 60); in Missouri, no change (18 vs. 18); in North

Table 1. Malaria Mortality and Morbidity in the U. S. by States for the year 1941.

State	Deaths	Rate/100,000	Cases Reported	Ratio of Reported Cases to Deaths
Alabama	120	4.2	4838	40.3:1
Arkansas	163	8.4	3426	21.0:1
Arizona	0	———	42	———
California	5	0.07	139	27.8:1
Colorado	0	———	2	———
Connecticut	0	———	10	———
Delaware	0	———	2	———
D. C.	13	1.7	1	———
Florida	85	4.4	145	1.7:1
Georgia	75	2.4	1122	15.0:1
Idaho	0	———	0	———
Illinois	8	0.1	111	13.9:1
Indiana	6	0.17	18	3.0:1
Iowa	0	———	20	———
Kansas	3	0.16	18	6.0:1
Kentucky	17	0.6	25	1.5:1
Louisiana	71	3.0	460	6.5:1
Maine	0	———	0	———
Maryland	0	———	22	———
Massachusetts	1	0.023	10	10.0:1
Michigan	4	0.08	31	7.7:1
Minnesota	0	———	9	———
Mississippi	146	6.7	36,815	252.1:1
Missouri	25	0.7	59	2.4:1
Montana	0	———	1	———
Nebraska	0	———	1	———
Nevada	0	———	0	———
New Hampshire	0	———	0	———
New Jersey	0	———	13	———
New Mexico	0	———	36	———
New York	3	0.22	80	26.6:1
N. Carolina	32	0.89	237	7.4:1
N. Dakota	0	———	0	———
Ohio	5	0.07	15	3.0:1
Oklahoma	52	2.2	2030	39.0:1
Oregon	1	0.09	41	41.0:1
Pennsylvania	1	0.01	12	12.0:1
Rhode Island	0	———	2	———
S. Carolina	126	6.6	9830	78.0:1
S. Dakota	0	———	0	———
Tennessee	50	1.7	496	9.9:1
Texas	148	2.3	8068	54.5:1
Utah	0	———	0	———
Vermont	0	———	0	———
Virginia	3	0.1	73	24.3:1
Washington	0	———	8	———
*West Virginia	———	———	———	———
Wisconsin	1	———	1	1.0:1
Wyoming	1	0.4	2	2.0:1
Total	1390	.1055	68,289	

*(Excluding West Virginia) Report not received.

Total population of the U. S.—131,669,275 (1940 Census).

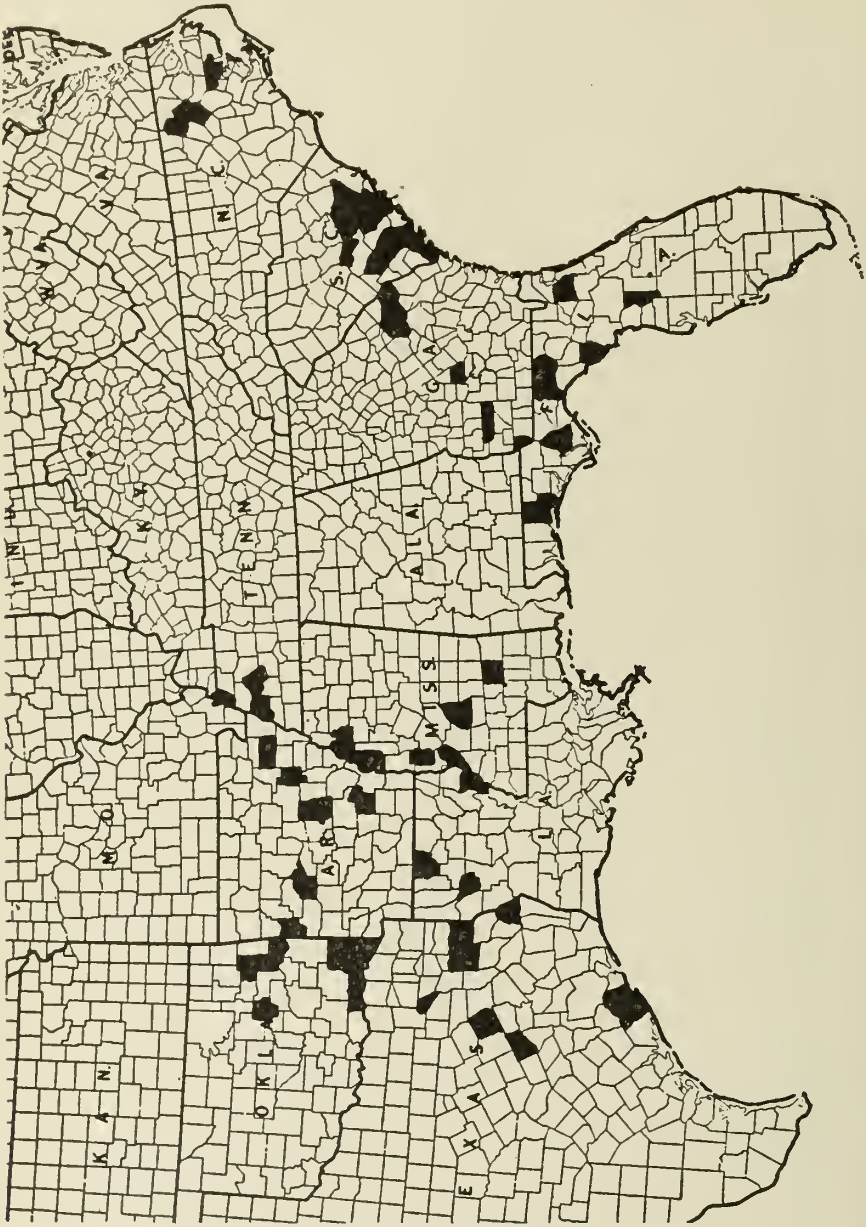

Figure 1. Malaria mortality rates per 100,000 population for fourteen Southern States (1929-1941), plotted semilogarithmically. The broken line is the average rate for the states concerned. Note that the rates for Arkansas, Alabama, Georgia, Florida, Louisiana, Mississippi, South Carolina and Texas, as well as the average rate, exceeded 10 during the 1933-1935 peak. The smaller numbers on the left-hand margin indicate the rate; those within the left-hand margin, on the right-hand and top margins refer to states.

Carolina, a decrease of 10 counties (16 vs. 26); in South Carolina, a decrease of 3 counties (27 vs. 30); in Tennessee, an increase of 3 counties (26 vs. 23); in Texas, a decrease of 5 counties (60 vs. 65), and in Virginia, a decrease of 2 counties (3 vs. 5).

No malaria deaths were reported in 1941 in the following twenty-one states: Arizona, Colorado, Connecticut, Delware, Idaho, Iowa, Maine, Maryland, Minnesota, Montana, Nebraska, Nevada, New Hampshire, New Jersey, New Mexico, North Dakota, Rhode Island, South Dakota, Utah, Vermont and Washington. Two deaths reported in Pennsylvania were certified as secondarily due to malaria. Three malaria deaths in Kansas were unreported since the origins of the infections were believed to be in Mississippi, North Carolina and Mexico. The single death reported from Wisconsin was stated to have been due to malaria contracted in Mexico; that in Wyoming, in Oklahoma.

Table 2. Malaria Mortality Rates of Southern States per 100,000 population.

State	1929	1930	1931	1932	1933	1934	1935	1936	1937	1938	1939	1940	1941
Ala.	16.3	11.3	8.2	6.9	10.0	10.8	11.9	12.0	7.9	8.2	7.6	7.0	4.2
Ark.	35.9	36.7	26.8	26.0	48.8	31.7	29.7	21.7	20.5	18.8	13.6	9.2	8.4
Fla.	32.0	22.5	13.9	15.5	24.9	29.7	20.7	21.8	11.4	11.2	7.6	5.2	4.4
Ga.	23.3	15.2	10.7	10.9	12.6	14.4	12.6	20.2	7.6	5.0	3.5	2.8	2.4
Ky.	1.6	2.1	2.1	1.5	2.9	2.4	3.0	1.8	1.0	1.2	0.8	0.63	0.6
La.	9.6	8.7	6.9	7.6	19.4	16.7	16.2	11.4	7.9	8.1	4.9	3.7	3.0
Miss.	15.8	14.1	10.5	16.2	34.4	32.3	25.9	16.4	14.0	12.4	10.5	7.6	6.7
Mo.	2.4	1.9	2.4	2.0	3.6	3.2	2.5	2.5	2.4	1.8	1.7	1.2	0.7
N. C.	2.1	1.4	1.5	1.6	1.2	2.4	2.6	4.2	2.6	2.2	1.7	1.7	0.89
Okla.	5.3	3.5	3.6	3.9	4.9	4.6	4.4	3.7	3.7	3.3	2.5	1.0	2.2
S. C.	21.3	19.2	13.6	13.1	12.8	19.8	23.8	25.2	14.2	12.1	9.1	6.7	6.6
Tenn.	6.9	5.4	5.3	4.6	9.4	9.4	7.7	5.3	3.6	3.6	3.3	2.1	1.7
Tex.	4.0	3.7	4.2	4.3	6.2	8.3	11.9	8.2	5.9	5.9	2.8	2.5	2.3
Va.	0.29	0.82	0.5	0.2	0.4	0.2	0.6	0.7	0.36	0.08	0.2	0.19	0.1
Av. rate	12.0	8.8	8.2	7.7	12.5	12.5	11.2	10.2	7.0	5.8	4.5	3.4	2.73

It will be of some interest and possible importance to indicate the counties with malaria deaths in 1941 which were responsible for rates of 25 or more, and those with apparently significant increases in 1941 over 1940. These are as follows and are respectively indicated by index letters [a] and [b]: in *Arkansas,* Lincoln[a], Lonoke[b], Perry[a], Poinsett[a,b], Sebastian[b], Woodruff[a,b], In *Florida*[a], Clay[a], Dixie[a], Jefferson[a,b], Liberty[a], Madison[a], Sumter[b], Walton[a,b],; in *Georgia*[a], Burke[b], Calhoun[a,b], Dougherty[b], Jefferson[b], Seminole[a], Wilcox[b]; in *Louisiana,* Claiborne[b], Red River[a,b], Tensas[b]; in *Mississippi,* Bolivar[a,b], Coahoma[b], Jones[b], Quitman[a], Rankin[b], Sharkey[a], Warren[a]; in *North Carolina,* Beaufort[b], Edgecombe[b], Halifax[b]; in *Oklahoma,* Cherokee[b], Chotaw[b], McCurtain[b], Okmulgee[b], Sequoyah[b]; in *South Carolina,* Bamberg[a,b], Beaufort[a], Berkeley[a], Calhoun[a,b], Clarendon[a,b], Colleton[a,b], Williamsurg[a,b], in *Tennessee,*

Crockett[b], Lake[a,b], Lauderdale[b]; and in *Texas,* Brazoria[b], Freestone[b], Panola[a,b], Rains[a], Robertson[a,b], Rusk[b], Sabine[a]. These counties are indicated in black on the spot map (Fig. 2).

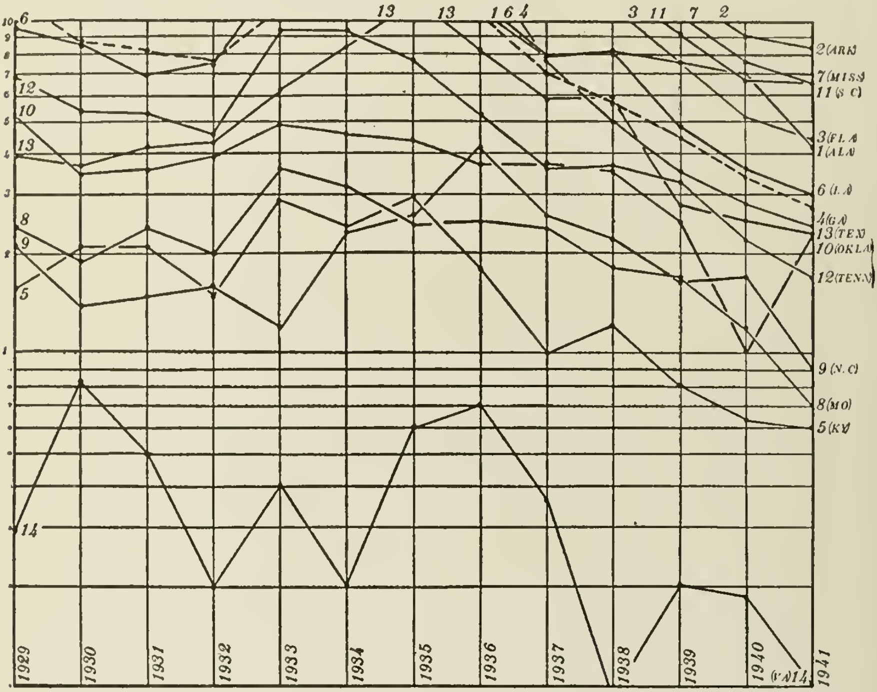

Figure 2. Spot map showing counties in the United States which had a 1941 malaria death rate of 25 or more per 100,000 population, or had apparently significant increases in the rate.

Malaria Morbidity.—The malaria cases reported for 1941 (Table 1) were disappointingly few (68,289), based on the expected ratio of 200 to 500 cases for one death. On this computed basis there were actually between 278,000 and 695,000 persons suffering from malaria during the year, or four to ten times as many as were reported. Of all the states reporting both deaths and cases, only Mississippi has furnished data which provide an expected ratio, 252,1:1. Eight years previously (1933) the ratio for this state was 103.8:1, (Faust and Diboll, 1935). Available comparable figures for other states are as follows: South Carolina, 47.8:1 (1933) and 78.0:1 (1941); Texas, 47.3:1 (1933) and 54.5:1 (1941); Virginia, 30.1:1 (1933) and 24.3:1 (1941); Alabama, 16.7:1 (1933) and 40.3:1 (1941); Tennessee, 16.6:1 (1933) and 9.9:1 (1941); Oklahoma, 13.7:1 (1933) and 39.0:1 (1941); Georgia, 13.1:1 (1933) and 15.0:1 (1941); Arkansas, 4.1:1 (1933) and 21.0:1 (1941); Ken-

tucky, 3.9:1 (1933) and 1.5:1 (1941); and Florida, 2.7:1 (1933) and 1.7:1 (1941). Thus, while some little progress has apparently been made in a few states in the accurate diagnosis and reporting of cases of malaria, the reverse is true in others. Certainly malaria morbidity reports are still undependable in the United States as a basis for judging the status of malaria.

Discussion

The 1941 reports reveal a continued decline, in malaria deaths which began in 1936 and have with few exceptions decreased year by year. The exceptions were Kentucky and Louisiana in 1938, Virginia in 1939, North Carolina in 1940, and Oklahoma in 1941. The slight increment in the rate in these states for the years indicated constitutes the only suggestion of the cyclic return to a peak now considerably overdue. It is possible that this resurge of malaria has been safely passed without having developed.

Counties shown in black on the map (Fig. 2) and representing present day moderately high malaria endemicity, or apparently significant increase in the death rate, do not correspond exactly with those on any previously published malaria mortality map. Attention is directed to the distinct improvement in the Southeastern Triangle of counties, in the Mississippi delta area and in the lower Rio Grande counties. On the other hand, it seems evident that dangerous extention has developed in Northeastern North Carolina, in central-south Mississippi, in central-east Texas and in central-east Oklahoma. Whether these 1941 potential danger zones will continue or increase in intensity or extent cannot now be determined, but these possibilities should be given careful attention.

Although there is little or no evidence from the data furnished that malaria morbidity in the Southern States is taken very seriously by laymen or physicians, there is an increasing interest taken by health authorities in several northern and eastern states in the source of malaria deaths and cases. This is a healthy sign and deserves commendation.

All of the information on which this report has been based has been obtained from civilian health authorities and concerns the civilian population. Malaria in the U.S. Army in the continental United States has rather consistently paralleled that of the civilian population but since 1918 has been considerably lower in cases and much lower in deaths. The former has been brought about by increasing prophylactic measures within the posts and in the immediate vicinity

of army camps, the latter by early and accurate diagnosis and treatment of cases. Cases in 1941 have been fewer than in the comparable year of 1917 (Simmons, 1942), while 1942 has been better than 1941. However, the participation of military personnel from Northern States in the Louisiana-Texas area maneuvers, in the early fall of 1941, was reflected in increased malaria cases in these troups on their return to quarters in the Fifth and Sixth Corps areas. This suggests that malaria is not necessarily declining but is only temporarily suppressed in endemic foci and awaits completely non-immune subjects for reactivation.

From another viewpoint, soldiers and civilian employees in tropical defense bases will be contracting malaria in tropical defense and combat areas and will sooner or later be returned to the continental United States as convalescent carriers. This will offer a potential opportunity for heterologous tropical strains of malaria plasmodia to become established in our midst. Thus in the near future a new malaria problem may significantly alter the present trend in reduced malaria morbidity and mortality in the United States.

Acknowledgements

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EMERGENT VEGETATION, MECHANICAL PROPERTIES OF THE WATER SURFACE, AND DISTRIBUTION OF ANOPHELES LARVAE*

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We know that the presence of emergent and semi-emergent aquatic plants and floating debris at the margins of standing waters favors the production of *Anopheles quadrimaculatus* larvae. This factor of the environment is highly effective. Where margins are clean and surfaces open, few larvae appear. Where shallows are filled with vegetation, the larval population is high. Practically speaking, a large fraction of the effort in control must be expended in reducing vegetation before larvicidal or naturalistic measures can be applied efficiently or with the assurance that they will be effective.

It is probable that emergent plants operate in many ways that protect and maintain the larval population. Some of these are obvious. Weeds form substantial barriers against wave action and limit violent agitation and grinding. They restrict the activities of predators. They break oil films and dust coatings. In the kind of world in which the *A. quadrimaculatus* larva lives, it is advantageous to find protective vegetation.

Larvae move freely and rapidly at the water surface. They are not fixed in the areas in which they are found. That they do concentrate in the vegetated, marginal shallows suggests that they are specially adapted for getting into and staying in this sort of environment.

The fact seems to be that the fitting of *A. quadrimaculatus* larvae into its special enviroment is a remarkable adjustment. It is unique in that the environment actively selects the animal. This will develop in the latter part of the paper.

Larvae may, as some have insisted, follow a chain of tropisms in searching out especially favorable vegetation. There is a large literature that deals with the relations of vegetation to production. It seems reasonable to suppose, too, that chemical properties of the water, conditioned by plant growth, might have much to do with the preferences of larvae. But our present knowledge of mosquito psychology and methods of analysis of the environment are scarcely ade-

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quate for an investigation of these. In experimenting, perhaps it may be better to start in doubting if the larva itself knows how it does it.

Explanations of natural phenomena in mechanical terms are uniquely satisfying. I have tried to find if the relation of larvae to emergent vegetation can be described in such elementary terms. To do this, I produce the mechanical equivalent of a patch of weeds, note how well the larvae like it, and try to understand why they like it. The results apply to field conditions only because my mechanical weed patch is in one important feature exactly like a real weed patch. This common feature seems to matter very much to the larvae in my experiments.

Anopheles larvae characteristically rest and feed at the water surface. They are supported by it. Plants and floating materials "bend" the water surface. This is the most readily observed feature of all emergent vegetation. How does this alteration of the normally flat surface affect the distribution of larvae?

Some plants bend the surface of the water upward, and some, downward. Stems and leaves that are "wettable" pull the surface about them into upward slopes, or positive menisci, and stems or leaves that do not wet readily bend it downward into negative menisci. Each emergent stem, dipping branch, or floating scrap is surrounded by a band of water that slopes upward or downward toward it. This is sketched in Figure 1.

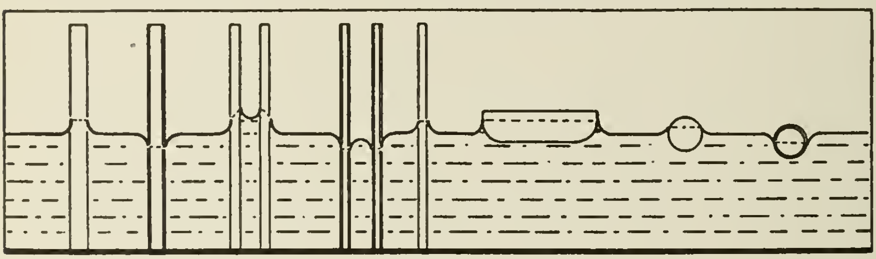

FIGURE 1

Most emergent plants are "wettable." The biological slimes that develop on their surfaces favor this; they produce positive menisci. A few freshly immersed, waxy stemmed plants and grasses do not wet readily, and form negative menisci. In time, all plants become slime coated and produce positive menisci where they break the surface.

The "mechanical weed patch" reproduces this effect of real plants. Glass rods wet like stems; if they are coated with fresh paraffin, they do not wet and become equivalent to waxy stems and floatage. The experimental weed patch consists of a pattern of glass rods

suspended from wooden bars (rods 3 mm. to 7 mm. in diameter) and dipping into the water. The bars and rods are spaced to make a neat stand of weeds five centimeters between centers, thirty "standard" weeds in fifteen hundred square centimeters of surface, and all in a series of enameled butcher's trays. See Figure 2.

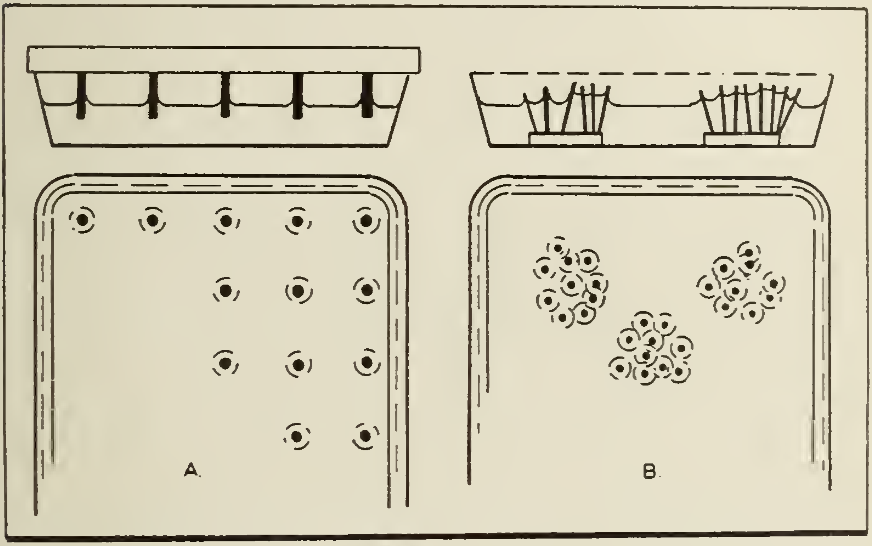

FIGURE 2

In each pan, then, there is an area of flat surface (about 75% of the whole, a lesser area of surface that slopes upward toward the sides of the pan and rods, and a still smaller area that slopes downward to the waxed surfaces. The water changes from flat to sloping water at 9 mm. from the emergent "weeds" and from the walls of the pans. This was made uniform by coating these surfaces with a solution of agar gel.

For our purposes it is much more instructive to see what happens to larvae in the vicinity of these synthetic weeds. Larvae touching them, are free to swing round and round. They may remove themselves with slight effort and move to other stems. There can be no fibre or adhesive attachment. Most larvae lie tail uppermost and seem happiest in this position. Frequently larvae move into the positive menisci head first, but they commonly swing round to the more comfortable position with a vigorous bend and snap. Once within the meniscus surface, considerable force must be exerted to dislodge them; gentle wind or light currents are inadequate. About negative menisci larvae orient themselves parallel to the curve of the upper surface.

When larvae swimming or floating at the surface of the water approach emergent stems they seem to be suddenly drawn into the meniscus by forces independent of their own efforts. The tail swings sharply toward the stem and the larva glides with increasing speed up the slope of the meniscus. This happens when the larva approaches closer than 9 mm. to the stem; precisely at the point that the flat surface gives way to the slope. This behavior suggests that surface forces of some sort are involved in orienting the larva.

The demonstration of these involves another model. If a small, larva sized, boat shaped piece of metal foil or celophane is bent sharply upward at one end and downward at the other and floated carefully at the water surface, a negative meniscus will be formed at the depressed end, and a positive meniscus will be produced under the upturn end. Now, if the boat is coaxed into the vicinity of a wetted stem, the end supporting the positive meniscus will move toward the stem. It will appear to be strongly attracted and will climb the meniscus as a live larva would.

Only the upturned, positive meniscus bearing end of the boat will do this. The end surrounded by a negative meniscus will be forced away with equal vigor.

When the boat approaches a waxy stem with a negative meniscus, opposite relations apply; the depressed end is attracted and the upturned end with a positive meniscus is strongly repelled.

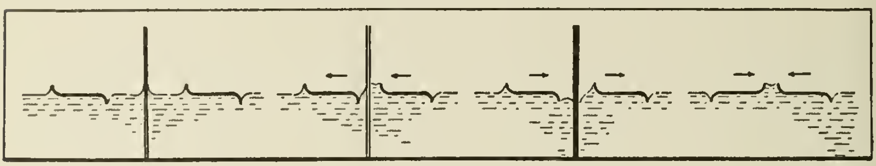

FIGURE 3

The forces involved here are the simple forces common to surfaces under tension. The water surface behaves like a stretched membrane, tending to keep the surface at minimum area. This "stretched" surface can be distorted into positive and negative menisci only by imposing forces perpendicular to the surface; wetted stems must lift this stretched sheet, and waxy stems must hang in it. But as long as the surface exists, it will present the smallest possible area.

When two positive menisci approach each other and merge, the area of the water surface decreases. The same is true when two negative menisci approach and join. But the surface area must be increased to allow the approach of a positive and negative meniscus.

This is shown in Figure 3B. The forces that maintain minimum surface area will separate them.

An *Anopheles quadrimaculatus* larva normally rests with its dorsal side uppermost. Parts of the submentum, the palps, thoracic hairs, palmate hairs, and spiracular plate are unwetted. They bear the load of the mosquito and produce negative menisci. The spiracular plate, with its fringe of fine, short spines, resists wetting very markedly, but its posterior borders wet readily.

When the plate is tilted forward the wetted posterior border is raised slightly above the surface and a positive meniscus is formed. It is possible that larvae may control this to their advantage, but it may be shown that larvae that have been killed by very gentle heating behave in the same way. The tail-borne positive meniscus is forced toward the apex of the plant produced positive meniscus by the forces maintaining minimum surface area.

That the larva is oriented and confined in an area of emergent vegetation where it is protected from rough weather, hungry fish, and oiling crews is incidental. It is fortunate for the larva, of course. But the water surface itself is more "satisfied" with the arrangement.

Within the past year Dr. Archie Hess and co-workers in the Division of Health and Safety, Tennessee Valley Authority, have demonstrated the fundamental relations of emergent vegetation and larval densities in areas controlled by water level fluctuation. The experiments given above confirm the marked positive relation between the "intersection index" and larval numbers in test waters, and add force to the already recognized value of aquatic vegetation control in anti-malarial operations.

DISTRIBUTION OF LARVAE IN ARTIFICIAL WEED PATCH

	No. Larvae In Batch	No. Per 100 cm.² on Flat Surface	No. Per 100 cm.² on Positive Menisci	No. Per 100 cm.² on Negative Menisci	Ratio Flat Curve
i	143	5.2	18	15	3.5
ii	154	4.2	18	44	4.9
iii	156	6.7	17	6	2.3
iv	131	5.2	17	18	3.3
v	130	5.3	17	15	3.2
vi	139	2.3	15	37	7.8
vii	103	3.6	21	19	5.8
viii	121	3.6	15	50	5.7
ix	114	2.3	21	31	9.8
x	126	2.0	20	56	12.6
xi	77	1.3	23	17	17.0
xii	84	1.8	21	20	11.5
xiii	82	2.3	18	25	7.7

Ratio of densities, curve/flat in all trials—5.6

Total Area	1428 cm.²
Flat Area	1074 cm.² (74%)
Sides (positive)	250 cm.² (18%)
Weeds (positive)	52 cm.² (4%)
Weeds (negative)	52 cm.² (4%)

DISTRIBUTION OF LARVAE IN ARTIFICIAL WEED PATCH

	No. Larvae in Batch	No. Per 100 cm.^{2} on flat Surface	No. Per 100 cm.^{2} on Positive Menisci	Ratio Curve Flat
i	98	3.0	17	5.7
ii	118	3.2	22	6.8
iii	113	2.9	21	7.3
iv	125	2.4	26	10.6
v	72	3.0	10	3.5
vi	100	2.2	20	8.9
vii	103	.8	24	31.5
viii	114	1.3	26	20.6
ix	115	2.0	24	11.9
x	117	2.7	23	8.4
xi	106	2.0	22	10.7

Ratio of densities, curve/flat in all trials—9.2

Total Area	1428 cm.^{2}
Flat Area	1037 cm.^{2} (73%)
Sides (positive)	250 cm.^{2} (17%)
Weeds (positive)	141 cm.^{2} (10%)

STUDIES ON THE MODE OF ACTION OF QUININE IN AVIAN MALARIA*

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*Presented at the Joint Session of the National Malaria Society and the American Society of Tropical Medicine, Richmond, Va., Nov. 12, 1942.

During the last decade we have learned that quinine influences the respiration, the rate of growth and the nuclear division of the malaria parasite. However, the question whether it is quinine itself or a metabolite of quinine which exerts these influences is still unanswered. Lourie (1934) suggested that a metabolite was involved, but considered the evidence, from somewhat unsuitable material, indecisive. The discovery of *Plasmodium lophurae* by Coggeshall (1938) and its transmission to the duck by Wolfson (1940) have made available an inexpensive host, which is also large enough for work on quinine levels in the blood. The preliminary work reported here has investigated the possibilities of this infection and host in testing for the existence of an anti-plasmodial metabolite of quinine.

METHODS

The techniques of transfer, staining, counting, and estimating parasite number, synchronicity, and periodicity were the standard ones most recently described by Hewitt (1942). The infected blood was mixed with the usual citrated saline solution in a proportion of 1:3 to prevent clotting. Estimates of parasite numbers were based on counts large enough to ensure a standard error less than 10 per cent of the parasite number. Almost all the ducks used in the infection experiments were three to five week old White Pekins. A few domesticated mallards were also used in one experiment. The quinine determinations were performed by the Kyker, Webb, Andrews method* (1941). Only blood quinine levels were determined since Lourie's studies indicate that quinine acts directly on the parasite rather than on the immune reactions of the host.

Although the synchronicity of *P. lophurae* is low, preliminary studies showed that at about 4 A. M. on alternate days a large majority of the parasites are young trophozoites, i.e. less than half the size of the nucleus of the red blood cell they parasitize. There

*The services of Miss E. Lynch and Mr. W. E. Cornatzer in making the chemical determinations, and the technical assistance of Mr. L. Peasley and Miss M. Baker, are gratefully acknowledged.

is also a minimal number of old trophozoites and schizonts which are less susceptible to quinine (Lourie, 1934). The parasites were treated at this time in all but two preliminary experiments.

Quinine sulphate or di-hydrochloride was administered intravenously into the inner leg vein, the outer web vein, or the wing vein, thus avoiding individual differences in absorption rates. The dose of quinine was 60 mgs/kg, with quinine calculated as the free base. This high intravenous dose was only tolerated when injected at the rate of about 1.5 mgs/kg per twenty seconds. Blood for the quinine determinations was obtained by cardiac puncture, and in the older ducks the ossified sternum was trephined.

The reproductive rate of the parasites was used to determine the effects of the different treatments. This rate was obtained by dividing the parasite number present at a definite time after infection, by the parasite number initially present. Thus, if an initial infection of 19 parasites per thousand red blood cells increased to 300 parasites in three days, the reproductive rate would be 30x. (The standard error of the reproductive rate was determined by the formula for the standard error of a quotient). In order to facilitate comparisons, the reproductive rate of the control in each experiment was taken as 100 per cent, and the other reproductive rates were expressed as a per cent of the control rate. There is a minor disadvantage in this method when no reproduction occurs. The reproductive rate is then 1x, and expressing this as a per cent of normal gives a small positive value.

The transient effects of single doses of quinine (table 1)

Table 1. The Effects of Quinine Given before Infection on the Reproduction of *Plasmodium lophurae*.

Duck No.	Interval Between Quinine Injection and Malaria Infection	Increase in Time			
		2 days	2½ days	3 days	4 days
30	control	7.2x (100%)	9.5x (100%)	22.7x (100%)	38.3x (100%)
37	3¼ hours	1.1x (15.3%)	1.0x (10.5%)	1.5x (6.6%)	1.5x (3.9%)
25	4½ hours	5.4x (75.0%)	6.3x (66.3%)	12.3x (54.2%)	28.9x (75.5%)
34	5½ hours	1.7x (23.6%)	1.6x (16.8%)	2.0x (8.8%)	8.0x (20.9%)

Figures in parentheses equal $\frac{\textit{experimental increase}}{\text{control increase}} \times 100$.

necessitate the somewhat arbitrary choice of an end-point. Although a two day period approximates the normal length of the asexual reproductive cycle, the quinine effect often lasts longer. Consequently, the more sensitive three day period was chosen, but the trends

shown by use of either endpoint are very similar (table 1). Longer periods were not used, since reproduction may approach normal three days after treatment, and rates based on parasite numbers per thousand red blood cells would have to be corrected for the marked anemia near the peak of the infection (Hewitt, 1942).

The three day reproductive rate does not seem to be affected by large weight differences in the host. In one experiment the controls weighed 236 and 350 grams and their respective rates were 29.4x and 28.3x, while in another experiment controls weighing 174 and 418 grams had respective rates of 21x and 19.7x. The rate is influenced by differences in the intensity of the original infection, and in the percentage of multiply infected cells in the inoculum. In these experiments, most of the initial infections contained 1 to 3 parasites per hundred red blood cells, and about 10 per cent of the parasitized cells were multiply infected. The reproductive rates in the controls of various *in vivo* experiments varied from 20-29x. More rigid control of the above variables would probably reduce this variation. However, the use of percentage figures based on the controls of each experiment compensates for this variation and makes comparison between different experiments possible.

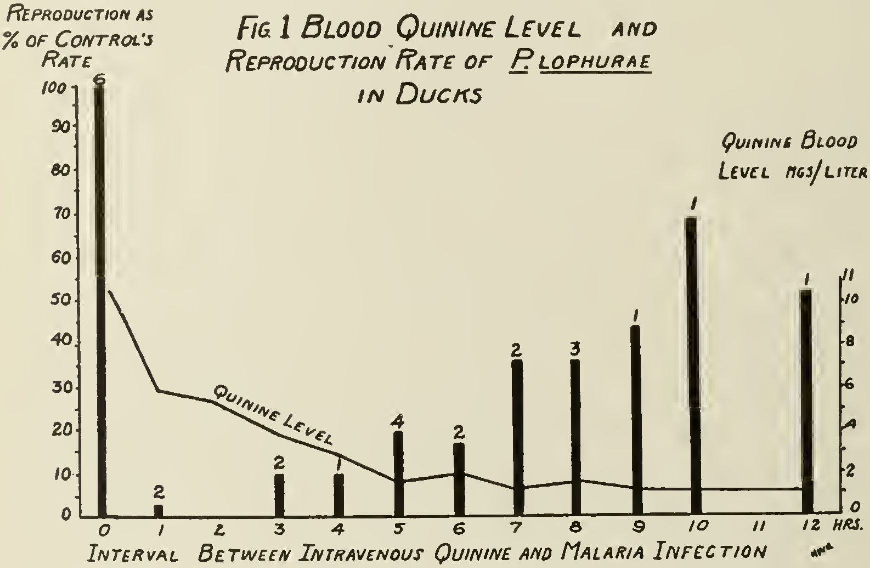
The Duration of the Anti-Plasmodial Environment in Ducks *Experiments* 1-4

The duration of the anti-plasmodial environment produced by quinine can be determined by giving birds a single dose of quinine and subsequently infecting them at various time intervals. The reproductive rates of these infections can then be compared with the normal rate and with the quinine blood level at the time of infection (figure 1, table 2). The use of the intravenous route of injection should exclude the possibility that persistent effects of a

Table 2. The Effects of Quinine Given before Infection on the Reproduction of *Plasmodium lophurae.*

Interval Between Quinine Injection and Malaria Infection	Average % Reproduction	Individual determinations
1 hour	2.25%	2.5% (½ hr.); 2% (1 hr).
3 hours	9.8%	13% (2¾ hrs.); 6.6% (3 1-3 hrs.).
4 hours	10.0%	10% (4¼ hrs.).
5 hours	20.0%	54.2% (4½ hrs.); 8% (4¾ hrs.); 5% (5 hrs.); 13% (5¼ hrs.).
6 hours	17.4%	8.8% (5-¾ hrs.); 26% (6 hrs.).
7 hours	37.0%	19% (6½ hrs.); 55% (7 hrs.).
8 hours	37.3%	14% (7½ hrs.) ; 66% (8 hrs.); 32% (8 hrs.)
9 hours	45.0%	45% (8½ hrs.).
10 hours	70.0%	70% (10½ hrs.).
12 hours	52.0%	52% (12 hrs.)

single dose might be due to slow absorption of quinine. Twenty-five birds were used in these experiments and their distribution among the different time intervals is given by the numbers above the histograms of figure 1. Determinations of parasite reproduction made



on several ducks at similar intervals show fair agreement, but the amount of variation increases with the time interval. This is not surprising in view of the relatively small number of determinations and the great individual variation in quinine levels. In all cases, the individual reproductive rates differ significantly from normal. The reproductive rate rises from zero at the start to somewhat over half the normal rate after the 12 hour interval. The duration of the anti-plasmodial envionment is thus at least 12 hours.

The blood level curve of quinine (figure 1 and table 3) is a composite one showing all our results following a single intravenous

Table 3. A Composite Blood Level Curve of Quinine in the Duck following 60 mgs/kg Quinine Intravenously.

Time	0	15 m.	30 m.	1 hr.	2 hrs.	3 hrs.	4 hrs.	5 hrs.	6 hrs.	7 hrs.
Average mgs/L	0.66	10.42	9.16	5.93	5.36	3.71	2.69	1.66	2.19	1.21
Range mgs/L	0.0- 1.24	8.03- 14.47	6.28- 12.09	4.16- 8.45	2.40- 9.69	2.22- 4.54	1.10- 4.03	0.96- 2.69	1.64- 3.20	1.08- 1.36
No. of samples	19	3	4	5	6	3	7	5	6	4
Time	8 hrs.	9 hrs.	12 hrs.	24 hrs.						
Average mgs/L	1.42	1.14	1.13	0.97						
Range mgs/L	1.06- 1.96	0.74- 1.67	0.91- 1.46	0.74- 1.34						
No. of samples	3	3	4	6						

dose of 60 mgs/kg. It combines a number of single determinations with a number of curves each comprising seven to ten determinations made at intervals on a single bird. The ducks used for the curves weighed about two kilograms, while the determinations of reproductive rate were performed on younger birds, weighing about 370 grams. However, single quinine determinations made on some of the younger birds do not indicate that the blood level of quinine is materially affected by weight differences or the repeated withdrawals of blood from the older birds. Each point on the composite curve (figure 1) is the average of three to seven separate determinations, many of which were performed in duplicate. At quinine levels below 2 mgs/L the average difference between duplicate samples was 0.3 mg/L, while in the range between 2-5 mgs/L the average difference was 0.5 mgs/L.

The curve indicates that the blood level falls rapidly, but that a limited amount of quinine may be present for at least eight hours after a single dose. The minor irregularities in the curve are due to small numbers and individual variability. Thus, the blood level of 2.7 mgs/L at four hours is based on seven birds whose levels ranged from 1.1-4.0 mgs/L. In general, a comparison between the quinine levels and the reproductive rates indicates a fairly close negative correlation, i.e. high quinine levels correspond to low reproductive rates, and low quinine levels to high reproductive rates. This is borne out by a study of the correlation coefficients in eleven of the birds whose reproductive rates are shown in the graph. In these birds, the quinine level was determined a fairly short time before the infected blood was introduced. The interval between quinine dosage and the malaria infection range from 4¼ to 8½ hours, the quinine blood levels from 3.93 to 0, and the reproductive rates from 2.3 to 29.4. The correlation coefficient between the quinine-infection intervals and the reproductive rates is -0.667 ± 0.167 and the correlation coefficient between the quinine levels and the reproductive rates was -0.866 ± 0.075. In the latter case, 75 per cent of the variability in reproductive rates was correlated with the variability in the blood quinine level.

However, this high correlation does not exclude the possibility that a metabolite of quinine, rather than quinine itself, is acting on the malaria parasites. It only excludes the possibility of a metabolite whose blood level differs markedly from that of quinine. The use of quinine-infection intervals exceeding twelve hours may yield important information. Such data could not be obtained because our chemical methods were inadequate at levels approaching 1 mg/L. Although the average of 19 control blood samples was 0.66

mg/L, six of the samples have ranged from 1.02-1.24 mg/L. Accordingly, the apparent quinine concentrations of 1.13 mg/L found at 12 hours, and of 0.97 mg/L at 24 hours, are open to question. A few determinations made on the quinine level of various organs and tissues showed that surprisingly high concentrations of quinine are present in the liver, the spleen, and the brain, even 8 hours after a single intravenous dose of 60 mg/kg. This suggests that a small amount of quinine may still be present in the blood after 12 hours. It is hoped that a more sensitive method will clarify this situation.

The Time Element in the Effect of In Vivo Quinine Experiments 5 & 6

Before performing *in vitro* experiments, it was necessary to know how long parasites must be exposed to the action of quinine *in vivo* before the reproductive rate is influenced. The absence of such data has made comparisons between the quinine concentrations effective *in vivo* and *in vitro* of limited value in the past. In experiment 5, an infected donor was given 60 mgs/kg of quinine intravenously. At intervals of 40 minutes, 1, 2, 3, and 4 hours, blood was withdrawn and inoculated into clean birds. Controls were obtained just before the quinine was administered.

The results (table 4 and fig. 2) show that an exposure of only 40 minutes to one hour reduces the reproductive rate to less than half of normal, while a 2 to 3 hour exposure reduces the rate to 10 per cent, and a 4 hour exposure prevents reproduction. The quinine concentration was not determined in the donor duck, but our composite blood level curve indicates that it was on the order of 11 mgs/L initially, and 3 mgs/L at the end of 4 hours. The initial blood quinine level was probably no higher than 15 mgs/L. The injection rate of 1.5 mgs/kg every twenty seconds yields a blood level of 15 mgs/L if blood is calculated as ten percent of total weight, and the fact that more rapid injections are lethal suggests that this

Table 4. The Effects of Various Time Exposures to *In Vivo* Quinine on the Reproduction of *Plasmodium lophurae.*

Hours Exposed	0	2/3	1	1½	2	2½	3	4
Experiment 5*								
Reproduction Rate (%)	100	31.5	43	—	11	—	9	5
Total birds	2	2	1	—	1	—	1	1
Experiment 6**								
Reproduction Rate (%)	100	—	—	41.5	30	23	22	—
Total birds	1	—	—	2	2	1	1	—

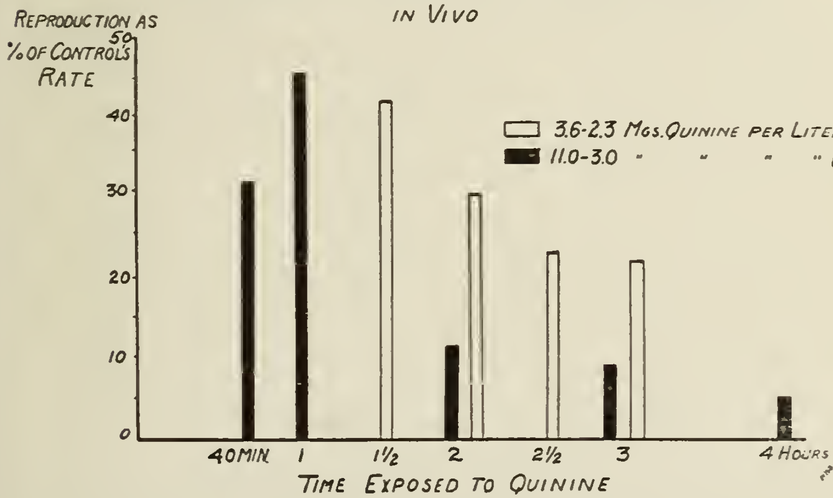
*Quinine blood level estimated as 11 mgs/L initially and 3 mgs/L after 4 hours.
** Quinine determined as 3.6 mgs/L initially and 2.3 mgs/L after 3 hours.

is the highest level possible. Furthermore, samples of cardiac blood withdrawn from two ducks when 50 and 85 percent of the total dose has been injected gave values of only 10.9 and 11.5 mgs/L, respectively. This agrees with the results of Hatcher and Weiss (1926) who state that 95 per cent of an intravenous dose of quinine leaves the blood of the cat and dog within five minutes.

In experiment 6, modification of the previous procedure permitted accurate determinations of both the initial and the terminal levels of quinine. Two hours after quinine was given to a clean bird a large quantity of infected blood was injected. Then at 1½, 2, 2½ and 3 hours after infection, blood was withdrawn and inoculated into clean birds. Quinine determinations made immediately before the quinine treated donor was infected showed a level of 3.64 mgs/L and those made after the last infected sample was withdrawn showed 2.31 mgs/L. As a control, a clean bird was infected with part of the blood used to infect the treated donor.

The results (table 4, fig. 2) confirm those of experiment 5. A dicided reduction of the reproductive rates occurred in the treated parasites, but in apparent correlation with the lower quinine level

FIG. 2 EFFECT ON REPRODUCTION OF P. LOPHURAE OF DIFFERENT TIMES OF EXPOSURE TO QUININE IN VIVO



in this experiment, the reduction is not as marked as in experiment 5. A two to three hours exposure resulted in a 3.7 times increase, in contrast to only a two fold increase in experiment 5. The results of both experiments demonstrate that two to three hours exposure *in vivo* depresses reproduction greatly.

In Vitro Incubation with and without Quinine. Experiments 7 & 8.

The effects of simple *in vitro* incubation were determined in experiment 7. A quantity of infected blood was incubated *in vitro* at 36° C. for various periods and then inoculated into clean birds. Although this is 5-6° C. below the body temperature of the duck, it was feared that higher temperatures might greatly reduce reproductive rates (Lourie, 1934). The incubation periods and the resulting reproductive rates, based on one bird each, were: 40 minutes —104%; 1¼ hours—126%; 1¾ hours—84%; 2 hours—92%; 3¼ hours—75%; and 4 hours—82%. This indicates that *in vitro* incubation for about 2½ hours will not depress reproduction markedly.

In our last experiment, No. 8, the effects of various quinine concentrations were determined *in vitro*. Different amounts of quinine in a physiological saline solution were added to 2 ml. samples of infected blood and incubated at 36° C. for 2½ hours. The blood was then inoculated into clean birds and the reproductive rates determined. The results are given in table 5 together with the comparable results of *in vivo* experiments 5 and 6. The only quinine concentration whose *in vitro* effects resembles the *in vivo* results was 500 mgs/L. It is striking that Lourie (1934) using a different criterion of antiplasmodial activity in the *P. cathemerium* infection of the canary, found that a concentration of 500 mgs/L was necessary for an *in vitro* effect, in spite of the fact that he also used a different temperature, 39° C.

Table 5. The Effects of *in vivo and in vitro* Quinine on the Reproduction of *Plasmodium lophurae.*

	Quinine mg/L	Duck No.	3 Day Reproduction: Actual	3 Day Reproduction: Exptl. / Avg. Control x 100
in vitro 2½ hours	500	141	1.2x	6.6%
		149	0.9x	5.0%
	250	142	13.8x	76.0%
		150	11.1x	61.2%
	100	135	17.3x	95.3%
		146	12.5x	68.9%
	10	139*	8.3x	45.7%
		144	16.0x	88.2%
	5	134	12.1x	66.7%
		137*	6.4x	35.3%
	0	138	15.8x	87.1%
		143	20.5x	112.9%
in vivo	11—4.5 (estimated)		2.02x	10.0%
2½ hours	3.6—2.3		3.74x	23.0%

*One leg diseased.

Many of the parasites treated with 500 mgs/L of quinine were abnormal soon after incubation, and after one day, 70 to 80 per cent of the plasmodia in birds 141 and 149 showed markedly abnormal morphology. These parasites were completely rounded; the cytoplasm was very dark blue; and the nucleus was indistinguishable. Such degenerate forms were also found in previous experiments, and in some of the other birds in this experiment, but never in such large numbers. In general, very low reproductive rates have been associated with a high frequency of abnormal forms, which increase during the first two days after treatment and then gradually disappear. Although the fate of parasites with comparatively slight abnormalties, such as large vacuoles, is uncertain, it seems probable that the extremely degenerate forms described above are dead.

The other results of experiment 8 are too irregular to warrant definite conclusions. Ducks 139 and 137 show reduced reproductive rates, but it is doubtful whether these are due to the quinine treatment, as they differ from the rates of the duplicate infections. The low rates may possibly be referred to a "diseased leg" condition which only appeared in ducks 139 and 137. Some of the weaker quinine solutions may have had a weak effect on reproduction, but reproduction in No. 135 treated with 100 mgs/L was higher than in one of the controls. The two controls are also not as similar as the duplicate controls of the *in vivo* work. The limited material in experiment 8 only permits the tentative conclusion that, to markedly affect the malaria reproductive rate, fifty to one hundred times more quinine is needed *in vitro* at 36° C. than *in vivo*.

Summary and Conclusions

(1) The reproductive rate of *Plasmodium lophurae* in the duck, during a three day period following the initial infection, is a sensitive and reliable indicator of the chemotherapeutic effects of quinine.

(2) There is a high negative correlation between the blood quinine level at infection and the subsequent reproductive rate when single intravenous doses of quinine are followed by malaria infection at various intervals. This indicates that if an antiplasmodial metabolite of quinine exists, its blood level curve must resemble that of quinine.

(3) The reproductive rate of *P. lophurae* is greatly inhibited by 40 minute to 4 hour *in vivo* exposures to the antiplasmodial environment produced by quinine.

(4) The reproductive rate is only reduced slightly by *in vitro*

incubation at 36° C. for two to three hours.

(5) Reproduction is inhibited by much lower quinine concentrations *in vivo* than *in vitro* at 36° C.

(6) There is no decisive evidence excluding the possibility that quinine may act indirectly through a metabolite.

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METHODS USED FOR INVESTIGATING CERTAIN HYDROLOGIC PROBLEMS RELATED TO MALARIA*

MELVIN H. GOODWIN, JR. AND LOUVA G. LENERT
From Emory University Field Station, Newton, Georgia

In 1939 there was initiated at the Emory University Field Station in Baker County, Georgia, a program of research designed to evaluate certain physical factors in their relation to malaria prevalence. The objectives were to study: 1) physical factors responsible for existence of ponds conducive to production of the local malaria vector, *Anopheles quadrimaculatus* Say, and 2) the probability of predicting the occurrence of malaria by the observation of certain natural phenomena.

Many of the data collected during the past three years ostensibly pertain more to hydrology than to malariology. It seems advisable to present a resume of the fundamentals of the program, indicating the inter-relations of the various phenomena under observation. Subsequent presentations of portions of the data may then be evaluated in their proper perspective. The methods of collecting these data have been obtained from various sources. Few were originated or developed in this program. Numerous accounts of the relation of malaria prevalence and natural phenomena have been presented. The present work was designed to supplement and expand information available. As far as we know, no previous attempt has been made to obtain information on all of the physical conditions described here and malaria morbidity in the same area.

Malarious regions have been variously described by physical aspects or by enumeration of types of breeding places of the specific vector or vectors of malaria in a particular section. The present discussion is limited to the southeastern United States, where the only known vector of malaria is *Anopheles quadrimaculatus*.

In the most recent account of the distribution of malaria in the United States, Faust[2] states that four endemic foci have been evident in the United States for the period 1929-1938. All of these lie within the physiographic province known as the Atlantic Coastal Plain[11]. Previously Boyd and Ponton[1] presented an account of the occurrence of malaria in the southeastern United States and indi-

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*Presented at the meeting of the National Malaria Society in conjunction with the Southern Medical Association, Richmond, Va., November 10, 1942.

The writers wish to express their sincere appreciation to Mr. M. T. Thomson, District Engineer, U. S. Geological Survey, Atlanta, Georgia, for his helpful suggestions and criticisms throughout the course of this work and for assisting with preparation of the manuscript.

cated a close relationship between the occurrence of malaria and lime sink and solution topography. Neither the areas described by Boyd and Ponton, nor the endemic foci indicated by Faust correspond strictly to the outcrops of any particular geologic formation. All lie within the Tertiary system formations and it seems appropriate to consider briefly some of the characteristics of this system.

Physiography of Malarious Regions in the Southeastern United States

The deposits of the Tertiary system in the southeastern states are extremely porous, soluble, and contain abundant supplies of water. There are four series, Eocene, the oldest, followed in order by Oligocene, Miocene, and Pliocene. Of the Tertiary series, the Pliocene deposits are known to be among the most important sources of water in the United States, with the Eocene, or Miocene ranking next. The majority of the most malarious areas lie within the outcrops of the Eocene series.

The extensive limestone formations characteristic of the Tertiary system are conducive to the development of the type of topography accompanying the heaviest breeding of *Anopheles quadrimaculatus.* Three types of depressions are formed, their final appearance depending on the depth at which solution takes place.

The first is the familiar lime sink which appears as a pipelike drain leading to a subterranean passage (Fig. 1-A). This formation

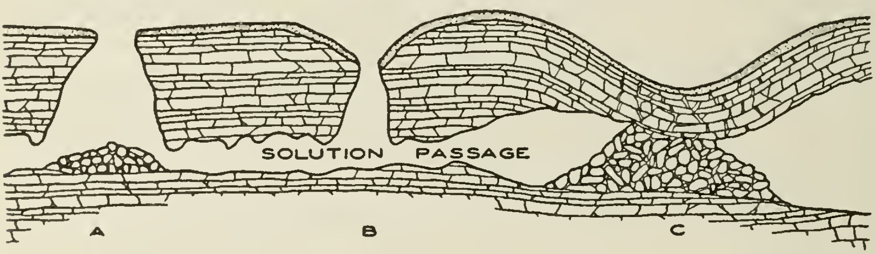

FIGURE 1

occurs when solution is affected by the downward percolation of ground-water through the interstices of the overlying rocks. As solution becomes more destructive, there is a complete collapse of the overburden and a passage is established from the ground surface to the water table. Immediately after formation, there is evidence of fracture around the periphery of the sink. The size of sink thus created varies from a few feet to several hundred feet in diameter.

Generally there is wide fluctuation in the height of water in the sink, reflecting actual variations in ground-water level.

Whether such depressions will hold water and thereby eventually breed *Anopheles quadrimaculatus* or not depends largely upon the nature of the surrounding terrain. If there is considerable drainage into the sink enough material will be washed in to partially fill the depression and obscure the connection to the water table, effecting a pond. With little drainage the limited amount of silt will probably be carried through the openings and clogging up will be slow, resulting in a dry sink.

Another type of depression is formed when solution is caused by influent seepage, with or without solution from below (Fig. 1-B). This sink is funnel-shaped with a drain extending to ground-water. This type of depression readily becomes a water holding basin. The formation was created by influent seepage from an existing drainage way and as materials continues to be washed in and accumulate, separation from the water table occurs.

The third type of depression results usually from subterranean solution at some distance below the surface. As solution becomes more extensive, support for the overburden is dissolved and a sag of material occurs when the roof of the solution cavity collapses (Fig. 1-C). There is no break through to the water table and a basin thus formed will generally hold water soon after its formation. Usually enough material is deposited within the basin to form a partially impervious layer. However, since the overburden is usually pervious material, enough seepage may occur to cause a break through to the water table forming a depression similar to one of the first two described.

The depressions described are dynamic, undergoing constant change. The general trend of the evolutionary process is toward extinction. The steps of ecological succession move toward formation of a pond or lake, then a swamp. Subsequently the swamp conditions are changed by more extensive plant encroachment and deposition of organic material, resulting in the formation of a bog. In the process of ecological succession conditions favorable for *A. quadrimaculatus* breeding may be created. This breeding will probably end in the swamp or bog stage as the water becomes more acid and large trees replace the shrubs and herbaceous plants.

Ponds on nearly level surfaces occur partially because the water table is high. The layer of semi-decayed organic material subsequently deposited acts as a sponge which absorbs water and tends to raise the water table still higher, furnishing additional water for solution destruction.

Relation of Ponds Breeding Anopheles Quadrimaculatus to Precipitation and Ground Water

Precipitation

Precipitation reaching the earth may be dispersed in four ways: 1) evaporation, 2) surface run-off, 3) seepage into the soil, and 4) surface storage in ponds, lakes, etc. When the rainfall rate exceeds the seepage or infiltration rate, storage and run-off are affected, the difference between rainfall and infiltration being the rainfall excess[17]. This excess provides water for surface storage. It also provides the surface run-off which may also replenish the ground-water under some conditions. Run-off is most likely to appear as surface run-off in streams. Initial detention is water required to wet the ground and vegetation, to fill small depressions and crevices not large enough to be important as storage reservoirs. The initial detention is usually lost by plant absorption or by evaporation.

Water is stored in three ways: 1) surface storage, already described, 2) ground storage in pervious material, and 3) artificial storage, e. g., impoundments.

Ground Water

The factor most closely related to surface storage other than precipitation is ground water. This may be static but is most often found in motion.

The relation between ponds and the ground water table varies considerably, depending upon the height of both and the topography of the surrounding terrain. In general, three relationships are recognized. There is the true perched pond, occurring rarely in this region, where the water is held in a basin of impervious material above the ground-water table (Fig. 2). The basin may be

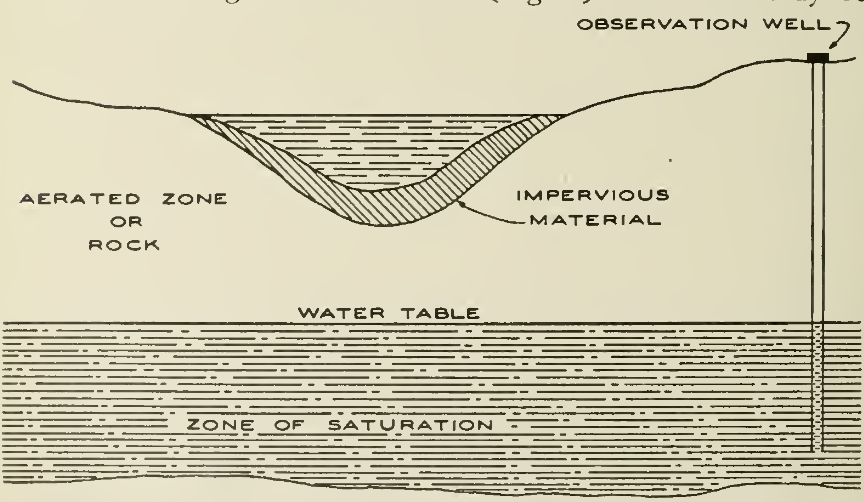

FIGURE 2

PERCHED POND

created either by a thin layer of impervious material over a pervious formation or may be a depression in an underlying impervious rock or clay formation.

The second type is the influent pond (Fig. 3). In this case the water is temporarily suspended above the water table. The basin is lined with semi-pervious material which allows seepage through the aerated zone of soil down to the water table.

The third type is the effluent pond in which the pond surface is actually a part of the ground water table (Fig. 4). Consequently the pond water is derived from the ground water.

Either of the two latter types may be transferred into the other,

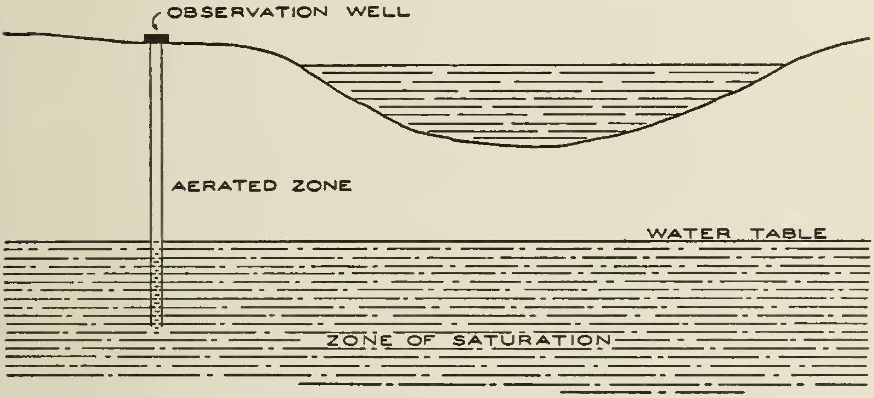

FIGURE 3

INFLUENT POND

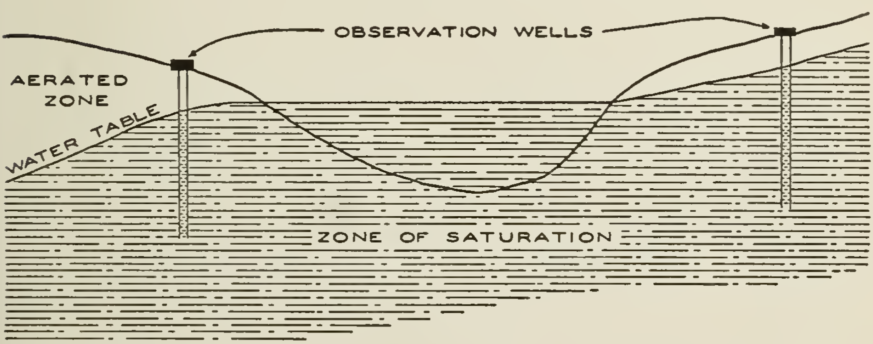

FIGURE 4

EFFLUENT POND

depending on the amount of water present, i.e., ground water may rise to intercept the water in the pond or may fall below the pond level.

Thus, to investigate adequately the occurrence of ponds which breed malaria-carrying mosquitoes, we must observe the natural conditions which assure their existence at the proper time for such breeding.

Methodology

The Area Selected

The area selected for this study is located in a highly malarious section of southwest Georgia. Various other observations concerned with anopheline biology and malaria morbidity are being made in addition to the work described here. The collection of data described is also concerned with many of these problems.

Maps were prepared of the entire drainage area in which was located the sector under observation. Phenomena occurring in any part of the drainage area might have an important relation to the observations in the specific section being observed.

Measurement of Rainfall

Precipitation on the area is measured with can-type rain gages, which are read daily. For measurement of rainfall intensity, automatic rain gages are used. The intensity of rainfall is very important in analyzing precipitation data[15]. It is obvious that torrential rains of short duration are unfavorable for influent seepage as they are accompanied by rapid run-off. Of course, this is modified by topography, vegetation and surface geology[13, 18].

It is necessary that rain gages be well distributed throughout the entire area as a rainfall record at any one point is inadequate to supply information as to the total rainfall affecting the area as a whole. The variation in the amount of precipitation from a single storm over a limited area is surprising, particularly for summer storms.

A method of anlyzing precipitation for use in studies such as this is to be presented elsewhere. It is sufficient to state here that the climatic year should begin at the end of the season of high temperature and intense evaporation[3, 4]. Little of the rain during the hot months of the year affects appreciably the ponds already existing.

Employing the method outlined above, the amount of water received by the area can be determined. The amount discharged from the area by run-off can also be determined.

Measurement of Run-Off

Discharge measurements of streams are made at the points where they enter and leave the drainage area and at other selected points within the area. Continuous records of stream flow are obtained by means of gaging stations equipped with water level recorders in simple shelters over stilling wells connected to the stream. Discharge measurements of each gaging station are made at as many heights of the stream as possible from which a stage-discharge relation curve or a "rating curve" is derived. Periodic discharge measurements must be made to definite changes in the state-discharge relation as they occur. The discharge in second-feet at any gage height can be determined from the "rating curve." It is possible to know the amount of water discharged at any time or for any interval of time from the stage record kept by the water level recorder and the "rating curve." Stream gaging is extremely complex requiring experienced personnel for collection and analysis of data. Detailed methods can be found in any text on hydrology; especially good accounts are given by Liddell[9] and Pickles[15].

A great deal of stream discharge data is collected by the Water Resources Branch of the U. S. Geological Survey. Publication of these data is found in yearly reports in the Water Supply Papers. Cooperation with the Geological Survey can usually be arranged through their District Engineer located in nearly every state, whereby stream flow stations can be jointly operated.

It would seem that a simple relationship exists between rainfall and run-off, but this is not the case because of variability of water used and amount of water received[5].

The amount of water used or stored in a drainage area is frequently expressed as the difference between precipitation and run-off. This difference is usually considered as water loss by most hydraulic engineers. In reality water used, or stored, is the difference between precipitation and losses by run-off and evaporation[21]. It may be in the form of ground water, surface storage, or plant use through transpiration.

Measurement of Ground Water

Ground water measurements are probably the easiest and most accurate of all hydrological measurements to make.

Wells which intercept the ground-water table but do not penetrate to deeper strata, are measured at regular intervals to determine depth of water below the surface. Suggestions for making these

measurements have been prepared by the U. S. Geological Survey in a Report of The Committee on Observation Wells[19].

At the beginning of this study, abandoned wells dug for domestic purposes were used for making measurements of ground water elevations. The bottoms of the wells were usually a few feet below the lowest ground water level. A protective curb, about three feet high, was built around the well, and a measuring point, made of one-fourth inch band-iron, bent at right angles, was firmly fixed to the curb. One edge of the portion projecting over the well was flattened to provide a knife-edge measuring point.

Wells dug for the specific purpose of measuring ground water are bored with a six-inch hand auger. In most cases, the ground is sufficiently hard to prevent caving after a depth of two or three feet and the well may be carried to a depth as great as forty feet in unconsolidated material. At the top where the soil is loose, a curbing of six-inch butt-joint drain tile is used. A concrete curb is cast in place extending about six inches above ground. A measuring point made from ¼" x 1" band-iron bent at right angles is incorporated in the curb. Precast covers are used to cover the opening, being held in place by a length of band-iron fastened to bolts cast into the curb (Fig.5). In very loose materials, sections of six-inch slip-joint stove pipe are riveted together and carried down as the well is cut. In this case, a four-inch auger is used to cut inside the stove pipe.

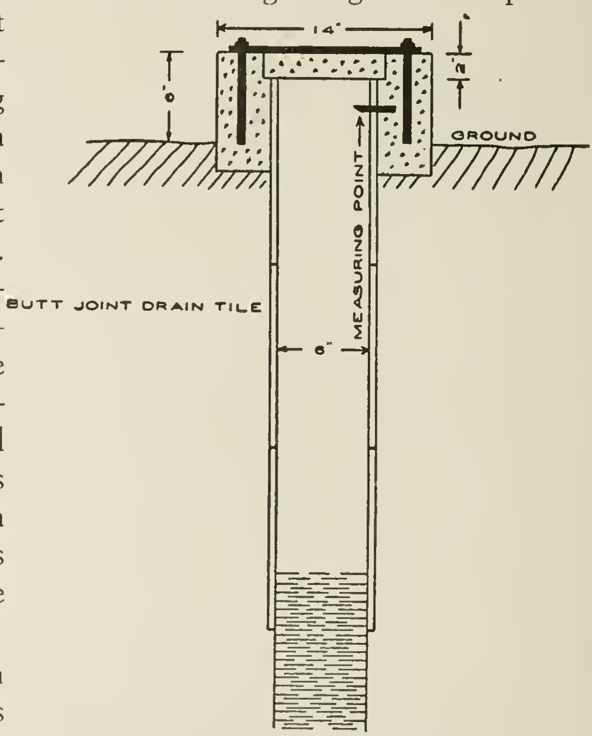

FIGURE 5
HAND BORED OBSERVATION WELL

Measurements in both types of wells are made by the wetted tape method,

using an ordinary steel tape graduated in hundreths of a foot. A weight is attached to the end of the tape and the first two feet chalked with ordinary carpenter's blue chalk. The weight and tape are then lowered into the well until the end of the tape is beneath the surface of the water. The tape is then read at the measuring point, and raised quickly, recording the total depth of tape and the height to which the lower end was submerged, the difference being the depth of the water below the measuring point.

Sea level elevation of each measuring point is determined by leveling so that all water level readings may be expressed in feet above mean sea level. By so doing the inter-relationship of all the ground water observation wells can be established.

The number of wells and their proximity is determined by topography, vegetation cover, and distance from exposed bodies of water.

Frequency of measurement is necessarily determined by amount of change, but weekly measurements are usually sufficient. Some wells are provided with water level recorders to provide a continuous record of the elevation of the water surface. It is not necessary nor is it especially desirable to equip all ground water observation wells with water level recorders.

Pond Level Measurements

Records of pond levels are made weekly from enameled staff gages installed in the ponds. This gage is graduated in tenths and hundredths of a foot, and the elevation of the pond is expressed in feet above mean sea level.

Where it is desirable to know the actual volume of water in a pond, an accurate six-inch interval contour map is prepared, and from this volumes are computed.

Evaporation Measurements

Evaporation measurements have not been deemed essential in this program. This is the termination of the hydrologic cycle where water is returned to the atmosphere. Measurements of evaporation and transpiration are admittedly inaccurate. Evaporation measurements are usually made as described by Kadel[6], with evaporation pan, stilling well and hook gage, or by a better method which employs an evaporation pan and measures the amount of water required to replace the volume to a fixed measuring point. Amount of evaporation is expressed in millimeters or tenths of an inch.

Summary

Methods employed to collect hydrological data pertaining to the occurrence of ponds in which *Anopheles quadrimaculatus* breed are discussed. All of the methods described, with the exception of the evaporation measurements, have been employed for the past three years at the Emory University Field Station on a selected area in Baker County, Georgia. The information is intended to serve as a background for future presentation of data collected by the procedures described.

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MINUTES—1942

NATIONAL MALARIA SOCIETY

Meeting Conjointly with the Southern Medical Association

Officers

Honorary President—Dr. L. O. Howard, Washington, D. C.

President—Mr. John H. O'Neill, New Orleans, La.

President-elect—Brigadier General James S. Simmons, Washington, D. C.

Vice President—Dr. Harold W. Brown, Chapel Hill, N. C.

Secretary Treasurer—Dr. Mark F. Boyd, Tallahassee, Fla.

Tuesday, November 10, 2:00 *P. M.*

The National Malaria Society convened in joint session with the Sanitary Engineers' and Sanitation Officers' Section, Southern Branch, American Public Health Association, at the auditorium of the Y. M. C. A., Richmond, Virginia, and was called to order by the President, Mr. John H. O'Neill, New Orleans, Louisiana.

The president appointed the following temporary committees, viz: nominations and audit. The president, in the absence of Colonel Charles F. Craig, the editor, formally presented to the Society the initial volume of "The Journal of the National Malaria Society", which had just made its appearance from the press.

Thereafter Mr. O'Neill gave his presidential address on "The War and Our Opportunity for Service," which was followed by a symposium of eight papers dealing with "Malaria Control in War Areas," and a further scientific paper unrelated thereto. On the completion of this program there was a brief recess, after which the Society reconvened in business session.

The minutes of the 1941 meeting held in St. Louis, Missouri, were approved as published in Volume one of the Society's Journal.

The secretary-treasurer submitted the following report on membership:

From the 1941 roster of 204 honorary and active names, three members have been lost by death, and 17 dropped for non-payment of dues. There have been 22 active members gained by election, a

current total of 207. Of these 125 are in good standing as of date of the report.

The following financial report was also submitted, viz:

Balance as of Nov. 12, 1941	$364.94
Receipts from delinquent, current and advance dues, interest and subscriptions . . .	434.48
Total	$799.42
Expenditures before paying for Volume one of the Journal	151.41
Balance as shown by bank book . . .	$648.01

It was further reported that $300.00 of the above was earmarked for the payment of the initial volume of the Journal, and that it was confiidently expected that before the end of the calendar year sufficient funds to guarantee the availability at least a similar minimum for the publication of Volume two.

Thereupon Mr. J. L. Robertson, Jr., on behalf of the auditing committee, reported that his committee had audited the account of the secretary-treasurer and found them correct, and introduced a motion, which was adopted, that the report be accepted and an honorarium of $50.00 be allowed the secretary's assistant.

Mr. Nelson H. Rector then presented recommendations from the committee on resolutions, which resulted in the adoption of the following resolutions, viz:

a) Whereas, our Country is engaged in a global war, requiring the utilization of all knowledge possessed by our citizens, and

Whereas, military activities are increasing in the tropics where malaria is a severe hazard, and

Whereas, the National Malaria Society has incorporated in its membership outstanding malariologists,

Therefore be it resolved that the President of the National Malaria Society be empowered to confer with representatives of the several United States Services with regard to the selection from the membership and to appoint a committee of qualified and acceptable members of the Society consisting of a physician, a sanitary engineer and an entomologist, to cooperate with the Army, the Navy, and the Public Health Service and to make available to them the technical skill and knowledge possessed by the members of the National Malaria Society.

The remaining resolutions have the following substance and tenor:

b) Relating to the death of the following members, Dr. R. W. Hegner and Dr. W. C. Sweet.

c) That the annual meetings consist of three sessions, not more than two of which shall be held jointly with other organizations.

d) That in the event the Southern Medical Association does not meet during 1943, the question of a 1943 session of the Society shall be settled by the incoming president, Brigadier General James S. Simmons, M.C., U.S.A.

e) The thanks of the Society to the Richmond Academy of Medicine and the Y. M. C. A.

f) Directing the secretary to express to Colonel Charles F. Craig the thanks and appreciation of the Society for his editorial work, and their wishes for his speedy recovery: and an expression of the Society's good wishes to Mr. J. A. LePrince.

The secretary-treasurer further discussed plans relating to the development of the Society's Journal. A motion was adopted authorizing the secretary to distribute gratis not more than ten copies of the Journal to desirable indexing and abstract Journals.

The committee on nominations offered the following slate, viz:

Honorary President—Dr. L. O. Howard, Washington, D. C.
President—Brigadier General J. S. Simmons,
Washington, D. C.
President-Elect—Mr. G. H. Bradley, Atlanta, Georgia
Vice President—Mr. J. L. Robertson, Jr., Memphis, Tenn.
Secretary-Treasurer—Dr. Mark F. Boyd, Tallahassee, Fla.

There being no nominations from the floor, a motion was adopted directing the secretary to cast the unanimous ballot of the Society for the nominees.

The Society then adjourned to 2:00 p. m. Thursday.

Thursday, November 12, 2:00 *P. M.*

The National Malaria Society convened in joint session with the American Society of Tropical Medicine at the auditorium of the Y. M. C. A., Richmond, Virginia, Mr. J. H. O'Neill, President, National Malaria Society, and Dr. Ernest Carroll Faust, President, American Society of Tropical Medicine, presiding.

A program of nine papers was presented at this session.

There being no further business, Society then adjourned *sine die.*

TOTAQUINE AND THE CONSERVATION OF QUININE

By Henry E. Meleney, M.D.*

The necessity of conserving stocks of quinine for the use of the armed forces during the present war has been recognized by the United States government, and the following steps have been taken in the program of conservation.

The War Production Board issued "Quinine Order M-131" which "froze" stocks present in this country and restricted the use of quinine and other cinchona alkaloids to the treatment of malaria, except that quinidine could also be used for the treatment of cardiac disorders.

The War Production Board, through the drug trade, urged that all unopened packages of quinine be returned to the manufacturers for government use, and an effort is being made to bring in opened packages as well.

The United States Food and Drug Administration, on recommendation from the Subcommittee on Tropical Diseases of the National Research Council, established a minimum content of cinchona alkaloids in so-called "chill tonics" equivalent to a daily dosage of 20 grains of quinine. This represents an increase over former requirements and made such products more effective in the treatment of malaria.

The United States Pharmacopeia, in its Twelfth Edition 1942 recognized Totaquine as an antimalarial preparation. After this edition had gone to press it appeared advisable to set more accurate standards for Totaquine in order to assure a fair degree of uniformity of the product. After a conference attended by representatives of the Pharmacopeia, the government, National Research Council and the manufacturers, a definition of Totaquine was accepted by the Pharmacopeia requiring not less than 7% and not more than 12% of anhydrous quinine and a total of not less than 70% and not more than 80% of onhydrous crystallizable cinchona alkaloids, these cinchona alkaloids to include cinchonidine, cinchoninine, quinidine and quinine. This definition permits the use of Latin-American cinchona barks which are relatively low in quinine content.

The subcommittee on Tropical Diseases of the National Research Council, after a study of the literature on Totaquine ex-

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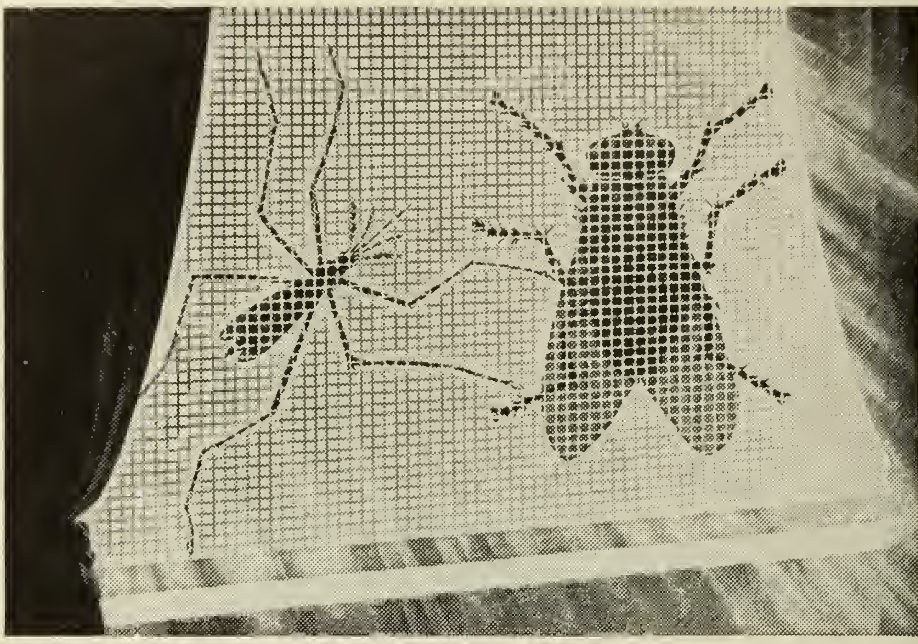
*Chairman, Subcommittee on Tropical Diseases, Division Medical Sciences, National Research Council. Presented at the meeting of the National Malaria Society, November 12, 1942

pressed the opinion that it could be used in the oral treatment of malaria with equal effectiveness to quinine sulfate if employed in equal or slightly larger doses.

As the supply of Totaquine increases an effort will be made to educate the medical profession to its use for the oral treatment of malaria in the civilian population, thus permitting quinine to be reserved for the armed forces. Quinine dihydrochloride, however, will also be available for civilian cases in which parenteral therapy is necessary.

Henry E. Meleney, M.D.



TOTAQUINE MERCK

an official
U.S.P. Antimalarial
for civilian use

Totaquine has been included in the Twelfth Revision of *The United States Pharmacopoeia* as an official U.S.P. preparation for the treatment of malaria.

• • •

Totaquine Merck, U.S.P. XII, is a mixture of alkaloids from the bark of *Cinchona succirubra* Pavon and other suitable species of Cinchona. It contains not less than 7 per cent and not more than 12 per cent of anhydrous quinine, and a total of not less than 70 per cent and not more than 80 per cent of the anhydrous crystallizable Cinchona alkaloids.

• • •

Totaquine powder may vary somewhat in color, but is generally pale brown. Physicians accustomed to the pure white appearance of Quinine powder need not be disturbed by the color of Totaquine, as this has no bearing on the therapeutic properties of the drug. Totaquine is odorless and has a bitter taste. It is practically insoluble in water, but is readily soluble in dilute mineral acids. It is neither hygroscopic nor efflorescent. The incompatibilities of Totaquine are similar to those of Quinine Sulfate, but Totaquine is not incompatible with alkali, calcium or magnesium carbonates, or their oxides, or hydroxides.

• • •

Totaquine Merck, U.S.P. XII, is available in powder form for prescription purposes. Totaquine is also available in tablet and other pharmaceutical forms, ready for immediate dispensing, under the labels of leading pharmaceutical manufacturers.

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